Fault detection in glucose control: Is it time to move beyond CGM data?

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Abstract: People with diabetes mellitus type 1 could benefit from fully automated systems for glucose control. However, faults in any component of the system can severely compromise the safety of the user. An increasing degree of automation also increases the risk that faults remain undiscovered for longer periods – unless automated routines for fault detection are implemented at the same time.
The aim of this article is to give a categorized overview of methods for fault detection in glucose control systems. This overview targets at disclosing hidden potentials for improvement and unresolved issues.
Methods for fault detection in glucose control systems have been reviewed and classified with respect to categories such as the type of method and the exploited data basis. Both journal and conference papers were taken into account.
Compared to the number of studies on glucose control algorithms, only a few articles have been published on fault detection. Surprisingly few of them consider system information beyond the standard diabetes care data.

Keywords: Biomedical systems; Fault detection; Fault diagnosis

1. INTRODUCTION

Glucose control is an essential part of daily life for people with diabetes mellitus type 1 (DM1). Because of destroyed insulin-producing cells in the pancreas, a person with DM1 has to regulate the blood glucose level (BGL) manually. Technological advancements have been achieved that help affected people: continuous glucose monitors and pumps for continuous insulin infusion are available nowadays. The subcutaneous (SC) tissue is commonly used for both insulin infusion (I_{SC}) and glucose sensing (G_{SC}). The automation of these systems is the next goal of many research groups. Increasing automation requires an increasing degree of reliability because users will naturally pay less attention to the correct functioning of a system that is supposed to work automatically.

Figure 1 shows a simplified sketch of the units of an artificial pancreas (AP). Input into the AP is the real glucose concentration (G_{real}) at the sensor location. The sensing unit transmits the measured glucose concentration (G_{measured}) to the controller unit where the intended insulin infusion rate (IIR_{intended}) is determined. Based on that, the insulin infusion unit injects the real insulin infusion rate (IIR_{real}). As indicated here, the measured glucose concentration differs from the real glucose concentration. The same applies to the intended and the real insulin infusion rate.

These discrepancies are potentially dangerous when the deviations become too large; since a correct dosing of insulin is not longer ensured even if the controller unit is working fault-free.

Faults can occur in all units of the artificial pancreas and require various actions. It is important to understand the potential occurrence and impact of a fault in order to address it adequately. A systematic risk analysis guides to this understanding. Based on that knowledge, suitable fault detection and diagnosis functions can be developed. The number of publications on fault detection is slightly increasing over the years as figure 2 shows. The total number per year, however, is still very low given the effort put into clinical studies to test closed-loop control algorithms. This paper categorizes published methods for fault detection and diagnosis in glucose control systems to provide an overview of available work for fellow researchers. Remarkably few investigated other sensors than continuous glucose monitoring (CGM) for fault detection.

2. FAULT DETECTION

A fault causes the system to deviate from its normal behaviour (Isermann, 2006). Communication dropouts, i.e. when the signal transfer between sensor and controller or controller and pump is disrupted, may be immediately noticed at the receiving unit by application of appropriate mechanisms in the communication protocol. Appropriate actions can thus be directly initiated upon those incidents.

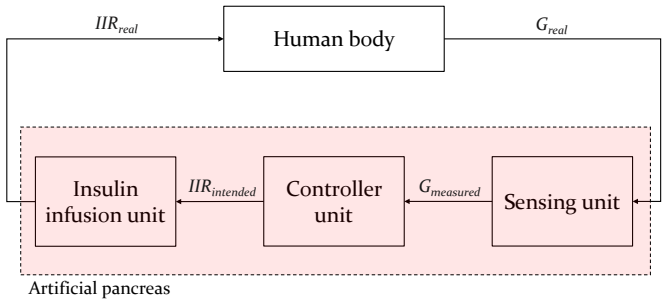

Fig. 1. Typical components of an artificial pancreas.

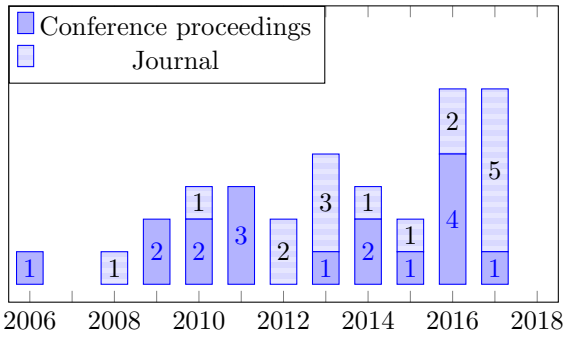

Fig. 2. Number of publications on fault detection in glucose control systems per year.

Other faults such as a disrupted insulin infusion have less obvious effects and require more complex detection methods.

Table 1 shows publications on fault detection in glucose control systems. Contributions in both journal and conference papers are considered, whereas posters and oral presentations at conferences and related abstracts have been omitted. Most of the publications address the $I_{SC}G_{SC}$ AP approach (i.e. SC insulin infusion and SC glucose sensing) for patients with DM1, whereas some deal with the treatment of hyperglycemia in critically ill patients. The intravenous route for insulin administration differentiates the intensive care unit (ICU) substantially from the outpatient setting. The ICU application was still included here because of the common use of G_{SC}. Table 1 classifies all methods of each study by several categories. One row of the table refers to one method in a publication. Thus, publications comparing different methods are listed more than once. More than one mark in the method category indicates a combination of different methods. Although a retrospective data analysis is originally reported twice (Bondia et al., 2008; Cescon et al., 2016), all methods in table 1 are generally suitable for real-time applications.

2.1 Fault modes

Fault detection in the AP has mainly focused on sensor and infusion faults. Among the sensor faults, *isolated spikes* and *transient negative bias* were addressed particularly often. Both fault modes were considered as intermittent faults. Isolated spikes are inherently random signal abnormalities rather than permanent sensor failures. The negatively biased sensor signal is usually transient because its major given cause is lost sensitivity due to pressure induced sensor attenuation (PISA) during night, which ceases as soon as the patient moves and the pressure is relieved. Zhao and Fu (2015) used steps to model isolated spikes and a biased signal. Generic signal anomalies (positive and negative steps, exponential changes and drift, and random noise) were analyzed by Turksoy et al. (2015). Although those anomalies cannot be directly related to particular faults, they build a comprehensive basis for signal fault modeling in simulation studies. The question raised in four publications (Bondia et al., 2008; Tarin et al., 2010; Leal et al., 2013b,a) is not a particular type of CGM faults but whether the sensor readings are faulty or fault-free.

The studied fault modes of the insulin infusion unit are *no delivery*, *under-delivery* and *over-delivery*. Although different faults are claimed to cause no delivery and under-delivery, i.e. disconnection (Baysal et al., 2013b; Herrero et al., 2012), leakage (Herrero et al., 2012), and complete (Facchinetti et al., 2013) or partial occlusion (Del Favero et al., 2014; Finan et al., 2010; Rojas et al., 2011b,a; Vega-Hernandez et al., 2009a), a further differentiation into fault causes seems not favorable here since the faults are not further examined after detection.

2.2 Methods

We differentiate between *process model based* and *signal based* methods. Process model based methods use a model of the process to reveal the occurrence of a fault by e.g. analytical redundancy. Signal based methods can be purely threshold based and reveal a fault when a process variable exceeds a given threshold. Other signal based methods are process history based: statistical or non-statistical features are extracted from historical data with known states (Venkatasubramanian et al., 2003). New data with unknown state is analyzed by means of these features.

Signal based methods predominate over process model based methods in table 1. An explanation could be the challenge of modeling the process as accurately as needed for fault detection. The reported process model based methods take uncertainties into account by observing states with frequent input updates or estimating an interval of the states. Most of the more recently published methods, however, contain some sort of process history based analysis. This complies with the overall trend of exploiting information from data sources. Threshold checking of CGM data is rather used supplementary to confirm the detection by another method. An increased glucose concentration can, for example, confirm a disrupted insulin infusion (Howsmon et al., 2017).

2.3 Data input

All listed fault detection methods are based on CGM data. The insulin infusion rate, typically the "intended infusion rate", is also very common as information source, in particular to detect faults in the insulin infusion unit. Some methods require manual meal information by the user.

Apart from these standard measures in diabetes care, other data has been rarely considered. Only three different authors included data on the sensor status (Bondia et al., 2008; Tarin et al., 2010; Leal et al., 2013b,a) in their fault detection. The reason may be that the manufacturers

Table 1. Methods on automated detection of sensor and insulin infusion faults.

Reference	Fault modes: Sensor: Isolated spikes	Fault modes: Sensor: Negative bias	Fault modes: Sensor: Generic anomalies	Fault modes: Insulin infusion: No delivery	Fault modes: Insulin infusion: Under-delivery	Fault modes: Insulin infusion: Over-delivery	Methods: Process model based: Linear output observer (KF)	Methods: Process model based: Nonlinear state observer	Methods: Process model based: Interval state estimation	Methods: Signal based: Threshold based: Limit checking (CGM)	Methods: Signal based: Threshold based: Trend checking (dCGM/dt)	Methods: Signal based: Threshold based: Trend checking (d^2CGM/dt^2)	Methods: Signal based: Process history based: Statistical trend analysis	Methods: Signal based: Process history based: Bivariate classification	Methods: Signal based: Process history based: k nearest neighbor classification	Methods: Signal based: Process history based: Principal component analysis	Methods: Signal based: Process history based: Support vector machines	Methods: Signal based: Process history based: Discrete wavelet transform	Methods: Signal based: Process history based: Kernel density method	Methods: Signal based: Process history based: Locally weighted PLSR	Data input: Diabetes care: Continuous glucose monitoring	Data input: Diabetes care: Insulin infusion rate	Data input: Diabetes care: Meal information (manual)	Data input: Physical condition: Activity monitor data *	Data input: Physical condition: Body temperature	Data input: Physical condition: Septic status	Data input: Sensor status: Sensor current	Data input: Sensor status: Sensor current's rate of change	Data input: Sensor status: Registered voltage	Validation: Population: Diabetes mellitus type 1	Validation: Population: Intensive care unit	Validation: Period: Night	Validation: Period: Whole day	Validation: Data source: Clinical data	Validation: Data source: Simulation	Further information on method and/or data used for validation
Baysal et al. (2013b) 1				x						x											x									x		x		x		
Baysal et al. (2013b) 2				x			x														x	x								x		x		x		Multiple model estimation
Baysal et al. (2013b) 3				x										x		x					x									x		x		x		
Baysal et al. (2013b) 4		x					x				x	x									x									x		x		x		
Baysal et al. (2014)		x					x			x	x	x									x									x		x		x		Enlite™ glucose sensor (Medtronic)
Bequette (2010)	x						x			x	x										x									x			x			Not validated
Bondia et al. (2008)	faulty/fault-free																x				x						x	x	x	x			x		x	MiniMed CGMS MMT-7102
Cescon et al. (2016)					x								x								x	x								x			x	x		Anticipation of failures
Del Favero et al. (2013)	x	x			x		x(1)														x	x								x				x		
Del Favero et al. (2014)	x	x			x	x	x(2)														x	x	x							x			x	x		
Facchinetti et al. (2011)		x				x	x														x	x								x				x	x	FreeStyle Navigator (Abbott Diabetes), Omnipod system (Insulet Corp)
Facchinetti et al. (2013)	x	x		x			x														x	x								x				x	x	FreeStyle Navigator (Abbott Diabetes), Omnipod system (Insulet Corp)
Feng et al. (2016/2017)	x	x	x				x													x	x	x								x			x	x		Nominal angle analysis to differentiate faults from dynamical changes
Finan et al. (2010)		x			x											x					x	x	x							x			x	x	x	MiniMed CGMS (Medtronic)
Herrero et al. (2012)				x				x													x	x	x							x			x		x	
Howsmon et al. (2017)				x	x					x			x								x	x								x			x	x		Long/short term fault metric on glucose/insulin
Kovács et al. (2006)			x			x		x													x	x								x	x		x		x	
Leal et al. (2013a)	faulty/fault-free													x		x					x	x			x	(x)	x				x		x	x	I_{IV} G_{SC}, Guardian® REAL-Time CGMS (Medtronic)
Leal et al. (2013b)	faulty/fault-free																x				x	x				x	x			(x)	x		x	x	I_{IV} G_{SC}, Guardian® REAL-Time CGMS (Medtronic)
Mahmoudi et al. (2016a/2016b/2017)	x	x	x					x													x	x	x							x			x		x	Medtronic virtual patient model; Hardware redundancy for fault isolation [XX]
Rojas et al. (2011a) 1					x											x					x									x^c			x		x	G_{IV}
Rojas et al. (2011a) 2					x									x							x	x								x^c			x		x	G_{IV}
Rojas et al. (2011a) 3					x									x		x					x	x								x^c			x		x	G_{IV}
Rojas et al. (2011b)					x									x		x					x									x^c			x		x	G_{IV}
Shen et al. (2010)		x									x							x			x									x			x	x		FreeStyle Navigator (Abbott Diabetes)
Signal et al. (2012)	x										x								x		x									x			x	x		CGMS® System Gold™
Song et al. (2016)	x	x															x				x									x			x		x	Monitoring charts
Song et al. (2017)	x	x												x			x				x									x			x		x	
Tarin et al. (2010)	faulty/fault-free																	x			x						x	x	x	x			x	x		CGMS Gold (Medtronic)
Turksoy et al. (2015)			x														x				x									x			x		x	
Turksoy et al. (2017a)	x	x															x				x			x						x			x	x		Dexcom G4, BodyMedia Sense Wear Armband
Turksoy et al. (2017b)		x						x							x	x					x	x	x							x			x	x		Paradigm Veo Enlite system (Medtronic)
Vega-Hernandez et al. (2009a/2009b)					x	x		x													x	x	x							x			x		x	
Zhao et al. (2014/2015)	$x^{(2)}$	$x^{(2)}$															x				x									x			x		x	Monitoring charts

* Activity monitor data: heat flux, skin temperature, galvanic skin response, energy expenditure, 2D acceleration (Turksoy et al., 2017a)

Abbreviations: G_{IV} - intravenous glucose sensing, G_{SC} - subcutaneous glucose sensing, I_{IV} - intravenous insulin infusion, KF - Kalman filter, PLSR - partial least squares regression

Indices: [n]Newborns, [c]Children, [(1)]Facchinetti et al. (2011), [(2)]Facchinetti et al. (2013)

of sensing devices integrate fault detection themselves and advice the user to change the sensor upon detected long-lasting failure. However, control systems could also benefit from access to this information to adjust the control system's action before a fault has developed into a complete failure.

Body temperature and septic status have been considered for intensive care patients (Leal et al., 2013b,a). Data from an activity monitor was recently integrated into fault detection for DM1 to better know the patient's physical condition (Turksoy et al., 2017a). To our knowledge, this potential source for reliable fault detection has not been investigated by further academic groups.

3. DISCUSSION

3.1 Fault detection

Despite a great research effort on automation of glucose control systems, only few academic groups have published methods for fault detection.

Recent work focuses on the detection of sensor faults rather than infusion faults. This can be explained by the importance of reliable sensor information for the whole control system. Continuous glucose monitoring (CGM) data serves often as the sole basis for the control actions as well as for the fault detection and diagnosis in remaining components. A reason for disregarding the detection of insulin infusion faults might be that the SC dynamics deem a timely detection of insulin infusion faults challenging (Christiansen et al., 2017) if no other information than SC CGM data is available.

In one journal article, the authors integrate data from a fitness armband into a routine for fault detection Turksoy et al. (2017a). Given the recent popularity of fitness trackers it is surprising that no more research has been published on the use of health monitoring data for fault detection in glucose control.

3.2 Fault diagnosis

The distinction between actual component faults and disturbances is a challenge, and an appropriate trade-off between robustness and sensitivity needs to be established. Furthermore, physiological changes within the patient may be falsely classified as faults in other components and may result in misplaced triggering of safety functions. The detection of faults is clearly not enough to ensure the right control decision. Further knowledge about the fault is needed. General desirable characteristics of fault diagnostic systems are well described elsewhere (Venkatasubramanian et al., 2003). In the following, fault diagnosis in the AP is briefly discussed.

Fault isolation Isolability of different faults is one of the central desirable properties. It is not only of interest whether or not the system has a fault but also in which component the fault has occurred. Despite automatic system decisions, this information can assist the user in choosing the right action, e.g. changing the sensor rather than the insulin infusion set or vice versa.

Fault isolation is more ambitious than fault detection because it goes beyond the classification into "fault-free" and "faulty". Appropriate features have to be identified which allow to distinguish between faults.

The isolation of different faults of the same component, for example of two different sensor fault modes, has been achieved with several methods (see table 1). Only one research group aimed, however, to detect both sensor and insulin infusion set faults simultaneously with the same methods. The isolation of sensor faults, insulin infusion set faults and meal faults (meal estimation errors and meal-bolus faults) was realized by comparing CGM measurements with their predictions and confidence intervals (Del Favero et al., 2014).

Such threshold based methods have, however, a limited fault sensitivity, at least if thresholds are used exclusively on the glucose concentration. Narrower lower and upper thresholds increase the sensitivity but the required robustness against variability restricts this possibility.

Additional activity monitors, for example, can help to identify if dropping CGM values are caused by physical activity or PISA (Baysal et al., 2013a).

Fault identification Knowing that a certain fault has occurred, the next step of fault diagnosis would be to estimate the severity of a fault. Only one method of fault identification has been published. This method identifies the magnitude of altered insulin delivery (Vega-Hernandez et al., 2009a) and uses the information to adjust the insulin infusion rate accordingly (Vega-Hernandez et al., 2009b).

In medical applications, it is common to use consumables. The components concerned are therefore very likely to be exchanged after a fault has been detected and successfully isolated. This might be the reason why most methods published on fault diagnosis in AP end with fault detection. However, the magnitude of the fault may be determined as well to allow control adjustments to ensure safe operation despite the presence of faults. This can be useful, for example, when it is not possible to change the insulin infusion set immediately. Another example is a PISA: since this phenomenon is transient, a replacement of the sensor is not necessary. Nevertheless, the real glucose concentration is of interest for the control system.

3.3 Validation using simulations and clinical data

Computer simulations are often the first step to test new algorithms for fault detection. Various fault models are used for that. However, the published methods in table 1 have been tested under a variety of conditions including different simulators and cannot be directly compared with each other. Another challenge that occurs when one tries to compare different algorithms is missing information in publications, for example unreported values of model and tuning parameters. This renders an implementation and fair testing of different methods on the same data set almost impossible.

Clinical data are in general the gold standard to validate new methods. All investigators working with glucose control face the challenge that the effect of many faults is not immediately significant. The exact time of onset is often

hardly assessable nor is the fault source reported. Models of fault-free processes, on the other side, require large data quantities without faults. As it can become quite expensive to have experienced people reviewing large data sets, the community should probably work together to achieve a suitable data set.

4. CONCLUSION

Fault detection is an essential part of an artificial pancreas to guarantee safety at any time. Automated fault detection gained more academic attention in recent years. However, compared to the worldwide effort to achieve closed-loop glucose control, few publications deal with fault detection and diagnosis.

Methods on fault detection are based on continuous glucose monitoring data as standard, often supplemented by the intended insulin infusion rate. Future research should explore alternative ways of monitoring the state of the equipment and the physical condition of the user. For example, fitness trackers became generally very popular and should be further investigated.

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