Budapest University of Technology and Economics
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Development and Optimization of Glucose-Insulin System Models and Methods for Intensive Care Patients under Model-based Glycemic Control

Ph.D. Thesis Booklet

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1 Preliminaries and Objectives

Hyperglycemia (high blood glucose levels) is common in critical care since patients with no history of diabetes can develop stress-induced hyperglycemia. The increased counter-regulatory hormone and cytokine response stimulates endogenous glucose production and increases effective insulin resistance. Hyperglycemia has a significant impact on patient mortality, outcome and health care cost [Kri03; MMB01]. On the other hand, they are very unpredictable, and there is no consensus on what levels of performance can be obtained and how to achieve them.

Low insulin sensitivity, known as insulin resistance, and stress-induced surges in endogenous glucose production manifest as stress-induced hyperglycemia in critically ill patients. The increased counter-regulatory hormone and cytokine response stimulates endogenous glucose production and increases effective insulin resistance and it occurs primarily early in intensive care unit stay. Glycemic control has proven difficult [Cha+18b; Cha+11] due to the risk of hypoglycemia (low blood glucose levels) [Dos+08; Dun+10] and high levels of intra and inter-patient variability. Thus, safe, effective control has proven elusive, with clinical protocols often lacking patient-specificity and failing to consider inter/intra-patient variability [Le +10; Lin+08; Uyt+18]. There is thus a need for model-based patient-specific glycemic control solutions [Cha+18a; Cha+18b].

Glycemic control (GC) protocols directly capturing and controlling for patient-specific intra and inter-patient variability can reduce negative outcomes related to poor control and by limiting glucose levels to 6.1-7.75 mmol/L on average can cut mortality by 17-45% while also dramatically lowering other undesirable clinical outcomes including severe infection, sepsis, and septic shock, and polyneuropathy and multiple-organ failure ., as well as provide leading nutrition delivery and economic cost savings. However, they have been offset by a range of clinical trials using ad-hoc clinical protocols, which could not repeat early successful results.

The Stochastic TARgeted glucose control (STAR) protocol used in this research is a model-based glycemic approach [Eva+12], built on the same models used to develop and implement the SPRINT protocol, which was the only protocol to reduce organ failure, mortality and hypoglycemia. Relies on the Intensive Control Insulin-Nutrition-Glucose (ICING) model of fundamental Glucose-Insulin system dynamics [Lin+11], it directly captures inter- and intra- patient variability and drives clinically validated virtual patients. It is driven by a model-based patient-specific insulin sensitivity (SI), uniquely identified from clinical data, whose utility has also been clinically validated.

The objective of this research is to enable enhanced model-based glycaemic control through better modeling accuracy (reduce modeling error) by the implementation of enhanced and new parameter estimation methods and by analyzing and investigating several key model parameters such as insulin sensitivity, blood glucose levels, SI variability and endogenous glucose production (EGP) in different treatment phases, also address and track the inter-intra patient variability across different patient cohorts using a clinical data from 4 independent cohorts of 737 hyperglycemic critically ill patients treated by the STAR protocol in 4 different ICUs. Specifically Hungary, Malaysia, New Zealand, and Belgium.

2 Research Methods and New Results

Our research is done on the clinically validated STAR model-based glycemic control, which utilizes the Intensive Care Insulin-Nutrition-Glucose (ICING) model [Lin+11] to simulate the fundamental metabolic dynamics of the glucose/insulin system of the human body. The main 3 of 7 total equations are defined below where G(t) represents blood glucose, Q(t) represents interstitial insulin concentration, and I(t) represents plasma insulin concentration:

$$\frac{dG(t)}{\mathrm{dt}} = -p_G G(t) - S_I(t) G(t) \frac{Q(t)}{1 + \alpha_G Q(t)} + \frac{P(t) + EGP - CNS}{V_G}, \tag{1}$$

$$\frac{dQ(t)}{\mathrm{dt}} = n_I (I(t) - Q(t)) - n_C \frac{Q(t)}{1 + \alpha_G Q(t)}, \tag{2}$$

$$\frac{dI(t)}{\mathrm{dt}} = -n_K I(t) - n_L \frac{I(t)}{1 + \alpha_I I(t)} - n_I (I(t) - Q(t)) + \frac{u_{\mathrm{ex}}(t)}{V_I} + (1 - x_L) \frac{u_{\mathrm{en}}(t)}{V_I}, \tag{3}$$

All equations, parameters, inputs, and variables are defined in [Lin+11].

Insulin sensitivity, SI, is a key patient-specific parameter in the ICING model. During the patient's treatment, SI is identified hourly using an integral-based fitting method, and variability is assessed by the hour-to-hour change in SI levels. An SI profile over time can be used to create a virtual patient, which has been exclusively used in the design of GC protocols. Virtual trials on cohorts of virtual patients can evaluate GC changes and/or new treatment options before clinical use.

As it has been mentioned, the clinical data used in this study were collected from 4 independent cohorts of 737 hyperglycemic critically ill patients from 4 different ICUs. Specifically, 93 patients from Kalman Pandy Hospital, Gyula, Hungary, 216 from the International Islamic University Malaysia Medical Centre, Malaysia, 408 from Christchurch Hospital, Christchurch, New Zealand and 20 From the Centre Hospitalier Universitaire of Liège (CHU) ICU, Belgium. The selection criteria for patients were: (i) glycemic control of more than 60 hours; (ii) insulin administration at the beginning of the glycemic control; (iii) at least 10 BG measurements during the treatment. Diagnosed diabetic patients were excluded.

2.1 Estimating enhanced endogenous glucose production

Description of Thesis 1

One of the key elements and potential limitations of model-based glycemic control in general, and the STAR protocol in particular, is its assumed value for EGP. The assumed EGP value directly impacts the identified value of SI by directly contributing to the net glucose flux balanced by insulin-mediated glucose uptake. However, EGP cannot be measured directly in clinical care and relies on tracer studies with significant errors

in research. Hence, this value could be inaccurate and, critically, is not identifiable using clinically available data. Thus, significant error in the assumed value due to patient variability would bias identified SI and potentially limit control safety and efficacy.

In the current version of STAR, EGP is an a priori assumed, cohort-based constant, optimizing model performance across the entire cohort in all hours. However, in the identified SI profile for some patients, there are instances where SI hits its lowest levels (insulin resistance) and is constrained by the STAR model to a non-negative non-physiological lower limit, which results in a poor fit to BG measurements, potentially signaling the assumed value of EGP, at least in this case, is insufficient. This SI lower limit is two orders of magnitude lower than the clinical range, and when constrained to this level, it is an indication that the assumed EGP is too low for these given hours due to surging EGP. This issue typically occurs early in ICU stay and stress-induced hyperglycemia, where such bursts of EGP are common for some patient demographics. Notably, such problems are not unique to model-based control of adult ICU patients.

This thesis uses clinical data from 717 patients using STAR from 3 independent clinical cohorts to formally analyze the impact of the choice of EGP value on identified insulin sensitivity and the modeling accuracy of the fit to the measured clinical blood glucose data. In particular, when SI is at its lower limit, it is possible to find a higher EGP value leading to a better fit to BG data at a physiological SI value. The time and frequency of these events are important for understanding these cohorts and the physiological stress response, as well as reducing limitations to model-based GC.

A model-based EGP estimation method is developed to adjust the EGP according to the BG concentration and initially identify SI value when it hits the lower constraint limit. It elevates EGP from this initial value until the model can match the measured blood glucose levels. In particular, the elevated EGP value is identified using a simple least squares method minimizing the squared error between the linear interpolated blood glucose measurements and the simulated BG by the ICING model. The calculation was achieved based on the linear approximation of the not necessarily equidistant in-time blood glucose measurements. This estimated EGP is obtained:

$$EGP_{LS} = arg\,min_{EGP} \sum_{k=1}^{K} (G_m(t_k) - G_s(t_k, EGP))^2 \tag{4}$$

$$\text{such that EGP} \in [1.25, 3.5]$$

where t_k is the k-th time instant of the measurement with k=1,2,...,K and K is the number of measurements. G_s is the simulated blood glucose level, while G_m is the measured blood glucose level.

Results show that estimating a low EGP value where SI is close to the minimum value can cause bias in the identified SI value, which can limit the accuracy of the ICING model and potentially reduce the quality of GC treatment recommendation. In these cases where SI is constrained to a low minimum value, numbering 1-10% of possible hours and 23-63% of total patients in the three cohorts: Malaysian, New Zealand and Hungarian. 24-50% of these cases occur in the first 24 hours and 60-75% occur within in the first 72 hours. Estimating and adjusting EGP to a higher value using the proposed methods shifted SI for these hours to more physiologically acceptable values in the 3 different patient cohorts.

Estimating higher EGP significantly improved blood glucose fit to measured data and thus modeling accuracy, reducing the fitting error by 90% across the 3 different cohorts where 80% of the new estimated EGP value range was between 1.25-2 mmol/min, where fewer differences were seen in the rest 20% of higher range (2-3.5 mmol/min).

A further major result of this study, beyond the method presented, is the quantification of the potentially very wide range of EGP values in ICU patients, which may slightly exceed prior reports and remain to be prospectively verified.

Thesis 1

In this Thesis, I developed a new EGP estimation method to replace the cohort-based constant assumed value used in STAR protocol which is one of its limitations causing low modeling accuracy and bias in the key parameter insulin sensitivity level in some certain treatment hours. This method is only triggered when SI hits its lower minimum value, which is an indication of insulin resistance and potentially a surge in the EGP. The method elevates EGP from this initial value until the model can match the measured blood glucose levels, and I have achieved this by analyzing and using the clinical data of 717 ICU patients from 3 different cohorts. The outcomes of this thesis are as follows:

1.1 After analyzing SI levels of 717 patients using the standard cohort-based EGP level, I found that underestimating the EGP value when patients have insulin resistance, and SI is close to the minimum value can cause bias in the identified SI value, which will cause an error in the simulated BG thus limit the accuracy of ICING model and potentially reduce the quality of GC treatment recommendation.

1.2 I showed that these cases where SI is close to its low minimum value and indicating patients having insulin resistance, numbering 1-10% of possible treatment hours and 23-63% of total patients in the three cohorts: Malaysian, New Zealand, and Hungarian. Making it a very common situation, especially in the early ICU treatment where 24-50% of these cases occur in the first 24 hours and 60-75% occur within the first 72 hours.

1.3 By comparing the in-silico simulation results using the cohort-based EGP and the EGP resulted from using the proposed method, I demonstrated that estimating higher EGP using the developed method significantly improved blood glucose fit to measured data and modeling accuracy, reducing the fitting error by 90% across the 3 different cohorts where 80% of the new estimated EGP valuer range was between 1.25-2 mmol/min, where fewer differences were seen in the rest 20% of higher range (2-3.5 mmol/min).

1.4 A further major result of my research, beyond the method presented, is the quantification of the potentially very wide range of EGP values in ICU patients, which may slightly exceed prior reports, which can influence all the developed model-based glycemic control and remain to be prospectively verified.

The results of Thesis 1 are presented in Chapter 3 of the dissertation. Related publications are the following: [$j1$; $c4$] .

2.2 Practical scenarios for the clinical implementation of the new EGP estimation method

Description of Thesis 2

In Thesis 1, we assessed that one of the model's key parameters, endogenous glucose production (EGP), which is set to a fixed cohort-based value, is too low to represent the real physiological value of certain patients. A low minimum SI value is thus an indication that EGP needs to be raised to a higher value. By proposing a new EGP estimation method, results showed that increasing EGP enabled the model to follow the observed BG dynamics and surpass this limitation. Also showed impressive results in error reduction and change in the insulin sensitivity distribution. The next step is to assess the way how we can apply and include this new estimation method in the current STAR protocol step and real-time clinical treatment.

In this thesis, practical ways were suggested for the clinical implementation of the new EGP estimation method, as the proposed method keeps the new high estimated EGP until the end of the patient's treatment. By analyzing the time occurrence and duration of the low minimum SI (insulin resistance) episodes, will give a better understanding of how we can handle and manage the new high estimated EGP. Results were achieved using the same clinical data of 717 patients from 3 different ICUs used to develop the EGP estimation method.

Based on results, 83% of the low minimum constrained SI episodes happen within the first 96 hours, and 95% of it lasts for 3 hours. Based on these results, the most practical scenario to handle these situations is to keep the increased EGP estimated by the new method until the 4th day of treatment passed (if higher EGP was estimated on that period), after that period (first 4 days) if it happens again we may have to set back EGP to the initial fix cohort-based value after 3h each time we increase it.

In summary, the clinical implementation of the EGP estimation method presented can effectively capture and handle patients' EGP variability and avoid overestimating EGP for longer periods. We believe this will have a significant improvement to the model outcomes, and it will enhance glycemic control and create a space for further development and improvements.

Thesis 2

In this thesis, I analyzed the time occurrence and time lasting of the low minimum insulin sensitivity episodes in order to suggest a practical way how to implement the proposed new EGP estimation method in the STAR protocol and real-time clinical treatment. And the outcomes of this thesis were:

2.1 Initially, the EGP estimation method I proposed keeps the new estimated high EGP until the end of the treatment, and this may lead us to overestimate patients' EGP over time when patient health state improves.

2.2 I analyzed the time occurrence and time lasting of the low minimum insulin sensitivity episodes, and I found that 83% of these episodes happen within the first 96 hours and 95% of it lasts for 3 hours maximum.

2.3 Based on the results, I suggested that the most practical way to apply the new EGP estimation method is to keep the increased EGP estimated by the new method until the 4th day of treatment passed (if higher EGP was estimated in this 4-day period), after that period (first 4-days), if the method is triggered

and a higher EGP is estimated, we may have to set back EGP to the initial cohort-based value after 3h each time we increase it.

2.4 In another side analysis, I proved that setting the limit of EGP up to 3.5 mmol/min in the proposed estimation method shows a large reduction in BG fitting error to a very low value (2.33%) and a reduction of constrained SI values by 98%. Using EGP values higher than 3.5 mmol/min did not show any further improvement in the outcomes.

The results of Thesis 2 are presented in Chapter 4 of the dissertation. Related publications are the following: [*j*2; *c*4] .

2.3 Patients inter-intra variability in early stage of ICU stay

Description of Thesis 3

The clinical data shows the first 24h of patients' treatment after ICU admission is critical in glycemic control due to patient state variability and insulin resistance (low insulin sensitivity), resulting in high blood glucose levels (hyperglycemia), making glycemic control very sensitive in the early stages of intensive care unit admission.

In this thesis, we analyzed patient's insulin sensitivity levels (SI), SI variability (Δ SI), and blood glucose levels (BG) across the 3 different cohorts, and the aim of this work is to confirm the clinical expectation in one hand and to assess its potential impact on model-based glycemic control on the other hand, for that we examine the inter/intra differences in SI levels, SI variability and BG levels in the early stages of the treatment (first 24h hours of patient ICU admission) compared to the rest of the treatment time and the change in SI as the treatment progresses at the patient and cohort levels.

As expected, given the stress response physiology. Results aligned with the clinical expectations were the lowest insulin sensitivity values and the highest variability and blood glucose levels tend to be in the first 24h across all cohorts.

This thesis initiates the idea of implementing a customized model-based control explicitly designed for the early phase of patient treatment that can effectively handle patients' hyperglycemia and insulin resistance and patient state variability in the most critical and sensitive phase of patients' ICU treatment. Implementations such as higher glycemic target band, frequent measurements, more modulated insulin/nutrition intakes and better estimating the key model parameters such as estimating higher EGP as the proposed method in Thesis 1. These beneficial impacts may arise for STAR or any other model-based protocol from improved predictions and, thus, more accurate GC during treatment for early-stage treatments.

Thesis 3

In this thesis, I have initiated the implementation of a customized model-based control explicitly designed for the early phase of patient treatment that can effectively handle patients' hyperglycemia, insulin resistance, and patient state variability in the most critical and sensitive phase of their ICU treatment. For that, across 3 different cohorts, I analyzed patient's insulin sensitivity levels (SI), SI variability (Δ SI), and blood glucose levels (BG), and the aim of this work is to confirm the clinical expectation in one hand and to assess its potential impact on model-based glycemic control on the other hand, and the outcomes of this thesis were:

3.1 I confirmed, using the data set of patients treated by the STAR protocol, that the lowest insulin sensitivity levels and the highest variability/blood glucose levels tend to be in the first 24h across all cohorts. As expected, given the stress response physiology and these results align with the clinical expectations.
3.2 In this work, my aim is to open the door for the development of a customized model-based glycemic control of the STAR protocol or any other protocol explicitly designed for the early phase of patient ICU treatment.
3.3 The EGP estimation method I developed in Thesis 1 could be a good starting point as the early occurrence of hyperglycemia episodes is likely due to the surge in EGP seen particularly in severe sepsis and septic shock patients in the first 12-24 hours.
3.4 Other implementations could be a higher glycemic target band, frequent measurements, more modulated insulin/nutrition intakes, and specific estimating of the key physiological model parameters. These implementations need to be assessed in future research.

The results of Thesis 3 are presented in Chapter 5 of the dissertation. Related publications are the following: [*e*6; *e*7; *e*9; *e*5] .

2.4 Stochastic ICING

Description of Thesis 4

Most of the published models of the human glucose-insulin system are deterministic ones, i.e., ordinary differential equations models used to describe the physiological processes. These models do not take into account modeling of the uncertainty, system noise, and the stochastic nature of the physiological system [GPF11].

Intensive Care Insulin-Nutrition-Glucose (ICING) is one of the deterministic models that uses ordinary differential equations. This model is used in model-based glycemic control for critically ill patients under the Stochastic TARgeted (STAR) protocol [Lin+11; Eva+12; Fis+12].

SI is the key parameter when using the ICING model in the STAR protocol representing the 'whole body' metabolic state condition as a single parameter. The identification of the SI was achieved via an integral-based method. In this way, all the dynamic errors were lumped into the SI profile, which frequently caused high variability in the SI profiles and indirectly in the blood glucose levels. To solve this problem and try to regularize the SI profile, an additional stochastic term was suggested by Palancz et al. in [Pal+16] in the glucose equation, which can capture the unmodulated dynamics and measurement noise [Eva+12].

Palancz et al. in [Pal+16] investigated the stochastic Ito version of the ICING model (called ICING SDE) equations with parametric stochastic noise term. The computation of the system trajectories and their statistical futures were carried out using Runge-Kutta method with Wiener-type diffusion process term. Parameter estimation is achieved via the maximum likelihood technique. This type of stochastic model aims not only the characterization of the noise integrated into the stochastic term but also enables the reduction of the modeling error.

In this analysis thesis, the accuracy of the new stochastic version of ICING model was examined to assess it's potential use and implementation in the STAR protocol.

The modeling error was calculated and compared with the original version of the model (ICING) with a clinical data set collected during the treatment of 60 patients from three different ICU's in Belgium, Hungary, and New Zealand.

The results of this study indicate that the ICING SDE exhibited slightly lower modeling error compared to the original INCING model. However, the ICING SDE is unlikely to significantly impact treatment quality, and the high computational time and complexity of the stochastic modeling approach make it a less viable alternative at this time. Further research and improvements are needed before the ICING SDE can potentially replace the original INCING model.

Thesis 4

In this thesis, I analyzed and compared the new stochastic version of ICING model (SDE) to the original deterministic version (ODE) in order to examine it's potential use and replacement in the STAR protocol. This comparison was made by calculating the modeling error for each version with a clinical data set collected during the treatment of 60 patients from three different ICU's in Belgium, Hungary, and New Zealand., and the outcomes of this thesis were:

4.1 Based on the analysis results and comparison, I found that the stochastic ICING (SDE) was slightly more accurate than the deterministic one (ODE), and the modeling error was smaller.

4.2 I discussed that the new stochastic version of the ICING model is time and resources-intensive compared to the original version.

4.3 I concluded that the new version of the ICING model is not ready to replace the original version yet as the trade-off between the small improvement in the modeling accuracy and the complexity plus the time/resources needed to achieve that won't necessarily improve the treatment outcomes.

The results of Thesis 4 are presented in Chapter 6 of the dissertation. Related publications are the following: [$e5$; $e11$] .

3 Application of the New Results

The work presented in this research addressed several model-based glycemic control limitations and causes of modeling inaccuracy and suggested ways and methods to achieve better accuracy and handle patient variability.

Estimating variable higher EGP

The proposed EGP estimation method to be implemented in the current START protocol and to be applied in real-time clinical treatment, every hour will be analyzed, and the EGP will change only as needed and the method is triggered when SI hits its lower limit, starting each time from the assumed cohort-based value.

If a higher EGP is estimated within the first 4 days of treatment, it must be kept until the end of this period and if it is estimated after 4 days of treatment, the EGP value is set back to the original one after 3 hours passed.

This approach is not terribly computationally heavy and can be performed well within the 10-30 seconds required to make a treatment decision. Hence, it is not likely to affect compliance or ergonomics.

Customized model-based control for first 24h

Treating the first 24 hours differently by implementing a customized model-based control explicitly designed for the early phase of patient treatment in the most critical and sensitive phase of patients' ICU treatment.

New Implementations such as higher glycemic target band, frequent measurements, more modulated insulin/nutrition intakes and specific estimating of some of the key model parameters need to be analyzed and validated via in silico simulations.

The proposed EGP estimation method is a good starting point and by implementing it as discussed previously, it will b a good starting point for further customization and implementation of new features.

Stochastic modeling

Extending the ICING deterministic model with parametric stochastic noise term where the computation of the model trajectories and their statistical futures were carried out using Runge-Kutta method with Wiener-type diffusion process term. and the parameter estimation is achieved via the maximum likelihood technique. This process is computationally/ resource heavy and needs to be optimized. So the focus needs to be on improving the execution time either by generating fewer model trajectories (less than 100) or replacing the maximum likelihood with a simpler method.

4 Publication List

Number of publications:	11
Number of peer-reviewed journal papers (written in English):	3
Number of articles in journals indexed by WoS or Scopus:	3
Number of publications (in English) with at least 50% contribution of the author:	2
Number of peer-reviewed publications:	3
Number of independent citations:	9

4.1 Publications Linked to the Theses

	Journal papers	International conference and workshop papers	Local conference and workshop papers
Thesis 1	[$j1$]*	[$c4$]*	—
Thesis 2	[$j1$]*, [$j2$]	[$c4$]*	—
Thesis 3	[$j3$]	—	[$e6$],[$e7$],[$e9$],[$e5$]
Thesis 4	—	—	[$e5$],[$e11$]

* These publications are attached to multiple theses.
This classification follows the faculty's Ph.D. publication score system.

Journal Papers

[$j1$] Anane Yahia, Ákos Szlávecz, Jennifer L Knopp, Normy Norfiza Abdul Razak, Asma Abu Samah, Geoff Shaw, J Geoffrey Chase, and Balazs Benyo. Estimating enhanced endogenous glucose production in intensive care unit patients with severe insulin resistance. *Journal of diabetes science and technology* 16(5), 2022, pp. 1208–1219.

[*j*2] Anane Yahia, Balazs Benyo, and J Geoffrey Chase. Clinical application scenarios to handle insulin resistance and high endogenous glucose production for intensive care patients. *IFAC-PapersOnLine* 53(2), 2020, pp. 16299–16304.

[*j*3] Balázs Benyó, Béla Paláncz, Ákos Szlávecz, Bálint Szabó, Yahia Anane, Katalin Kovács, and J Geoffrey Chase. Artificial intelligence based insulin sensitivity prediction for personalized glycaemic control in intensive care. *IFAC-PapersOnLine* 53(2), 2020, pp. 16335–16340.

International Conference and Workshop Papers

[*c*4] Yahia Anane, Balázs Benyó, Ákos Szlávecz, Chris Pretty, and J Geoffrey Chase. Endogenous glucose production parameter estimation for intensive care patients. In: *2019 Scientific Meeting on Electrical-Electronics & Biomedical Engineering and Computer Science (EBBT)*, pp. 1–4. 2019.

Local Conference and Workshop Papers

[*e*5] Yahia Anane, Balázs Benyó, A Szlávecz, Béla Paláncz, and Geoff Chase. Potential use of the stochastic icing model in star protocol. In: *Proceedings of the Workshop on the Advances of Information Technology: WAIT 2019*, pp. 33–37. 2019.

[*e*6] Yahia Anane, Balázs Benyó, and Geoff Chase. Insulin sensitivity and blood glucose levels analysis of hungarian intensive care patients under model-based control. In: *Proceedings of the Workshop on the Advances of Information Technology (WAIT) 2021*, p. 123. 4. 2021.

[*e*7] Yahia Anane, Balázs Benyó, and Geoff Chase. Insulin sensitivity and blood glucose level analysis of critically ill patients in their early phase of icu treatment. In: *Medical Informatics 2020 - The XXXIII. Publication of the Neumann Colloquium conference*, pp. 157–166. 2020.

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[*e*11] Yahia Anane, Balázs Benyó, A Szlávecz, Béla Paláncz, and Geoff Chase. Accuracy assessment of the stochastic icing model using representative patient cohorts. In: *Abstract book for the 14th Miklos Ivanyi International PhD and DLA Symposium: Architectural, Engineering and Information Sciences*, pp. 47–48. 2018.

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