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Empirical Dynamic Model Identification for Blood-Glucose Dynamics in Response to Physical Activity

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Abstract

In this paper, the dynamic response of blood glucose concentration in response to physical activity of people with Type 1 Diabetes Mellitus (T1DM) is captured by subspace identification methods. Activity (input) and subcutaneous blood glucose measurements (output) are employed to construct a personalized prediction model through semi-definite programming. The model is calibrated and subsequently validated with non-overlapping data sets from 15 T1DM subjects. This preliminary clinical evaluation reveals the underlying linear dynamics between blood glucose concentration and physical activity. These types of models can enhance our capabilities of achieving tighter blood glucose control and early detection of hypoglycemia for people with T1DM.

I. Introduction

Type 1 Diabetes Mellitus (T1DM) is a metabolic disease caused by insufficient insulin production in the pancreatic beta cells. It is a major health problem around the world and approximately 19 million people are affected by this chronic disease [1]. T1DM can be managed by exogenous insulin administration; the goal of this treatment is to avoid hypo- and hyper-glycemia (low- and high-blood glucose concentrations). Proper administration of insulin can prevent long-term complications such as cardiovascular disease, nephropathy, neuropathy, and retinopathy caused by prolonged periods of hyperglycemia. Furthermore, it also can prevent immediate life-threatening conditions, such as coma and unconsciousness caused by hypoglycemia [2]. In current practice, physical activity for individuals with T1DM involves extensive preparation and close monitoring as it can cause hypoglycemia. Previously, physicians sometime advised against physical activity due to the high risk of hypoglycemia. However, as for people without T1DM, physical activity and exercise can improve the insulin sensitivity and reduce the risk of cardiovascular disease [3].

The physical activity has a dramatic effect on glucose regulation both in the near and long term. The latent effect of physical activity can cause hypoglycemia and nocturnal hypoglycemia even after several hours of the physical activity. Modeling the physical activity response in the blood glucose concentration is a major challenge due to inter- and intra-patient variability. Patient specific models may provide good results, but they are highly sensitive to the inpatient variability. On the other hand, population based models are robust, but their performance is poor compared to the patient specific models. Therefore, in this paper a hybrid approach is used where general system dynamics are identified for a population of T1DM subjects and some parameters, related to the gain of the system, are estimated using the data for individual subjects. Previously, Auto-Regressive models with eXogenous inputs (ARX) were used to represent unknown dynamics of blood glucose concentration of people with T1DM. However, there are many practical difficulties in identifying ARX models for blood glucose dynamics [4]. Typically, in such model identification, insulin infusion data are used as the only input variable and it has a direct effect on glucose control. However, there are many other variables that affect to the blood glucose concentration of people with T1DM, such as carbohydrate intake, physical activity, and stress level. The carbohydrate intake and the stress level are difficult to measure and quantify accurately. Therefore, those variables are hard to use in dynamical system modeling, especially considering that there is significant day-to-day variability in carbohydrate metabolism in persons with type 1 diabetes [5]. On the other hand, physical activity can be easily quantified by activity sensors, and these signals are available in real time.

Recently, multivariable adaptive closed-loop controllers have been developed to integrate different sensory inputs to the blood glucose control framework [6]. Adaptive system identification techniques have been used for blood glucose predictions to minimize hypoglycemia [7]. In these studies, physiological signals such as energy expenditure and galvanic skin response were used along with glucose measurements to construct multi-input single-output models. The correlation between physical activity and derivatives of the Continuous Glucose Monitoring (CGM) signals has been investigated via partial correlation analysis [8]. Positive and negative correlation of the physical activity to the first order derivative of the CGM has been observed for mild exercise sessions. Statistical techniques, such as principal component analysis, has been used in exercise detection to take precautions actions to avoid hypoglycemia [9]. These results confirm the importance of physical activity in capturing glucose dynamics.

Traditional system identification techniques, that use blood glucose (output) and insulin (input) data, have several limitations in capturing true dynamics. One of the major limitations is their inability to capture the variable delays in glucose sensors and insulin infusion with a relatively small model order. Most of the models used in blood glucose control algorithms assume fixed or no delay. Performance of models that only depends on subcutaneous glucose measurements and insulin infusion data are vulnerable to unmeasured disturbances.

In this paper, an alternative method to minimize those errors during and after physical activity is presented using a secondary physical activity-glucose model which can be used in

parallel with traditional insulin-glucose models. Since physical activity can be captured with minimum delay by using commercially available activity sensors, these enhanced models are especially important for children, adolescents, and athletes, who experience sudden changes in blood glucose due to their physical activity.

Human physiology is a complex system to model, and there are numerous unknown factors that can contribute to the blood glucose concentration. The inability to describe the effect of physical activity on glucose metabolism is considered one of the unsolved challenges in the development of artificial pancreas [10]. In this paper, black box identification techniques are used assuming a linear model structure for the underlying dynamics. Model order is determined by the Akaike Information Criterion (AIC) and subspace identification methods with stability constraints are employed for model development. Activity signal is used as the input to the system and blood glucose concentration is considered as the output. A state space model is identified for physical activity and blood glucose interaction. This approach helps to minimize the prediction error due to inherent delays associated with glucose sensors, which is roughly about approximately 15 to 30 minutes [11], when subjects are involved in physical activity. This formulation gives rise to a semi-definite programming problem that can be solved with standard convex optimization solvers.

The prediction accuracy of the developed models is validated with data from 15 T1DM subjects, which are independent of the model calibration data. Previously personalized population-based models without physical activity inputs were developed [12] and deployed in blood glucose controllers [13], [14]. In the proposed modeling technique, additional valuable information about blood glucose concentration that captures activity data are used to improve the predictive accuracy of blood glucose concentration.

This paper is organized as follows: The model development method is presented in Section II and model performance for 15 T1DM subjects is given in Section III. A brief discussion of the results and their applications are given in Section IV.

II. Method

A. Data Preprocessing

Subspace identification methods are popular in many practical applications, but there is still no unified framework for biological applications. Uncertainties, non-linearities and unmodeled dynamics pose serious challenges when they are applied to biological systems. The model developed in this paper was based on input and output measurements of activity levels and blood glucose concentrations. Blood glucose concentration was interpreted by the CGM readings (Dexcom G4, Dexcom, CA) that were obtained at five minute intervals and physical activity level was measured by commercially available activity monitors (Actigraph WGT3X-BT, Acti-graph, FL). Activity monitors produce three continuous signals proportional to the acceleration in the X, Y, and Z directions; they were typically sampled at a higher rate than the CGM signal. Both CGM and activity signals were processed by the vendor supplied algorithms to reduce noise and to remove non-physiologic values; thus, minimal processing was introduced in the data preprocessing stage. The variation of the activity signals can be larger than the CGM measurements due to their high sampling rate.

Therefore, activity signals were integrated over a one minute interval to obtain the total activity level during that time period. The magnitude of the activities was computed by the Euclidean norm of the X, Y, and Z acceleration measurements. These values were again filtered using a low pass filter and re-sampled at five minute intervals to be compatible with the CGM measurements. The cutoff frequency of the low-pass filter was chosen to attenuate the frequency components that were greater than the Nyquist frequency of the CGM sampling (0.0028 Hz). An eleventh order Finite Impulse Response (FIR) filter with a Hamming window was designed for this purpose and its delay was corrected by shifting the entire filtered output by five minutes without compromising the model's real-time prediction capabilities. Such a phase shift in filtered activity signal was necessary to align it with the CGM signal.

Data for 15 T1DM subjects were collected for this analysis through a standard clinical protocol given in [9]. Subjects were instructed to exercise for approximately an hour with mild intensity and then rest for several hours. Then they were asked to continue exercising for half an hour with moderate intensity. Exercise intensities were classified by a relative measurement called the Heart Rate Reserve (HRR) which is defined as the difference between the subject's maximum heart rate and resting heart rate. Each subject's maximum heart rate depends on their age, gender, weight and other physiological factors and is calculated using a well known formula in the sport and exercise literature [15], [16]. Mild and moderate exercises have categorized as 30% and 50% of the HRR.

Since the blood glucose level is affected by various other factors, data for model calibration and validation were chosen in such a way that they avoid such disturbances. For example, T1DM subjects are required to take large insulin doses known as boluses which is a major contributor to their blood glucose level. The effect of such insulin doses was minimized by avoiding them in the selected data windows. Activity signal was normalized by a nominal value to maintain the estimated parameters roughly within the same order of magnitude.

B. Model Order Selection

The model order for the system is obtained by the AIC, and AIC values of different model orders for both calibration and validation data sets are given in Figure 1. For this analysis, third order models provide the lowest AIC value. Generally, higher-order models were not preferred, because they may capture unwanted noise due to the limited number of calibration data points.

C. Parameter Identification

The state of the system $x(t)$ is chosen to be the current, one step ago, and two steps ago glucose values. The third order system dynamics are given by the discrete time system,

$$x(k+1) = Ax(k) + Bu(k) \quad (1)$$

where $x \in \mathbb{R}^{3 \times 1}$, $A \in \mathbb{R}^{3 \times 3}$, $B \in \mathbb{R}^{3 \times 1}$ and $u \in \mathbb{R}$. Activity signal $u(k)$ acts as the control signal for this system. In order to identify a generic model for the population of 15 T1DM subjects, the data is concatenated as follows,

$$X(1:n) = \begin{bmatrix} x_1(1:n) \\ \vdots \\ x_{15}(1:n) \end{bmatrix}^\top \quad U(1:n) = \begin{bmatrix} u_1(1:n) \\ \vdots \\ u_{15}(1:n) \end{bmatrix}^\top$$

where $x_i \in \mathbb{R}^{3 \times n}$, $u_i \in \mathbb{R}^{1 \times n}$, and $(1 : n)$ refers to the column 1 through n . Subspace identification method with stability constraint is used to obtain a stable system for blood glucose predictions. The subspace identification problem is formulated as

$$\min_{A,B} \left\| \left(X(2:n+1) - \begin{bmatrix} A & B \end{bmatrix} \begin{bmatrix} X(1:n) \\ U(1:n) \end{bmatrix} \right) W \right\|_F^2$$

where n is the number of data points, W is the weighting matrix, and $\|\cdot\|_F$ denotes the matrix norm. The method given in [17] is adopted to construct a two step optimization approach to get population dynamics with customized parameters for individual T1DM subjects. Asymptotic stability of the linear discrete time system (1) can be represented by the Lyapunov inequality. Then the parameter identification problem is transformed into a constrained optimization problem of the form,

$$\min_{A,B,P} \left\| \left(X(2:n+1) - \begin{bmatrix} A & B \end{bmatrix} \begin{bmatrix} X(1:n) \\ U(1:n) \end{bmatrix} \right) W \right\|_F^2 \quad \text{s. t. } P - APA^\top > 0 \quad \text{and} \quad P > 0$$

where $P \in \mathbb{R}^{3 \times 3}$. A small parameter $\delta > 0$ is introduced to ensure the existence of the solution.

$$P - APA^\top \geq \delta I \quad P \geq \delta I_n$$

Using the Schur complement, inequalities can be transformed into a compact form as given in (2).

$$\begin{bmatrix} P - \delta I & AP \\ PA^\top & P \end{bmatrix} \geq 0 \quad (2)$$

Let the weighting matrix W be in the following form with two new variables W_1 and W_2 ,

$$W = \begin{bmatrix} X(1:n) \\ U(1:n) \end{bmatrix}^\dagger \begin{bmatrix} PW_1 & 0 \\ 0 & W_2 \end{bmatrix}$$

where $V^\dagger \triangleq V^\top (VV^\top)^+$ and $^+$ denotes the generalized inverse. This decomposition allows us to optimize the matrix A and B independently. W is substituted into the objective function

$$\min_{A,B,P} \|X(2:n+1) \begin{bmatrix} X(1:n) \\ U(1:n) \end{bmatrix}^\dagger \begin{bmatrix} PW_1 & 0 \\ 0 & W_2 \end{bmatrix} - [APW_1 \quad BW_2]\|_F^2 = \min_{A,P} J_1(A,P) + \min_B J_2(B)$$

where,

$$J_1(A, P) \triangleq \|(K_1 - A)PW_1\|_F^2 \quad (3)$$

$$J_2(B) \triangleq \|(K_2 - B)W_2\|_F^2$$

$$\begin{bmatrix} K_1 & K_2 \end{bmatrix} \triangleq X(2:n+1) \begin{bmatrix} X(1:n) \\ U(1:n) \end{bmatrix}^\dagger. \quad (4)$$

The final form of the optimization problem takes the form

$$\min_A \|(K_1 P - AP)W_1\|_F^2$$

$$\begin{bmatrix} P - \delta I & AP \\ PA^\top & P \end{bmatrix} \geq 0$$

which is a quadratic with respect into the optimization variable. It can be transformed to the following linear programming problem with LMI constraints,

$$\min_{a,Q,P} a$$

$$a \geq J_1(A)$$

$$\begin{bmatrix} P - \delta I & AP \\ PA^\top & P \end{bmatrix} \geq 0$$

where, $Q \triangleq AP$ and $J_1(A) = \|(K_1 P - AP)W_1\|_F^2$. This problem is solved through CVX [18], [19] using the solver *SeDuMi* [20]. Note that objective function (4) has a closed form least squares solution. A two step optimization approach is used in this problem where at first matrix A is estimated using data from a population of T1DM subjects and then matrix B is obtained from individual subject data. Model performance is evaluated using average absolute error (e), defined as,

$$e = \frac{1}{n} \sum_{i=1}^n |\hat{y}_i - y_{\text{ref},i}| \quad (5)$$

where $\hat{y}$ and y_{ref} denote the blood glucose predictions and the actual measurements. This metric provides a clinical insight to how good or bad the predictions are compared to traditional metrics, such as R^2 , so that physicians can easily evaluate the benefits of derived models.

III. Results

The estimated system matrix A is given by

$$A = \begin{bmatrix} 1.9097 & -1.0816 & 0.1677 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix}$$

for the population of T1DM subjects and individually optimized control matrix B for each subject is given by $B = [b_i \ 0 \ 0]^T$, where the b_i elements are given in Table I. As examples, 30 minute blood glucose predictions for subjects 1 and 8 using calibration and validation data are given in Figures 2–5 in red squares. Duration of the physical activity, which is approximately one hour in the calibration data and half hour in the validation data are marked in gray. As a comparison, zero order predictions for 30 minute horizon are plotted in the same figures. Zero-order predictions are obtained by assuming no change in blood glucose level for the prediction horizon. As expected, the superior performance of the model is observed compared to the zero order predictions. The average absolute error for calibration and validation data for 5–30 minute prediction intervals are given in Tables II.

As a comparison, predictions of the insulin-glucose model given in [13] are given in Table III.

IV. Discussion

In this paper, a novel method to obtain a dynamic model for blood glucose dynamics for T1DM subjects in response to physical activity is presented. The experimental prediction results given in Table II show comparable error levels in both calibration and validation data sets which confirms no over fitting of calibration data. Table II also show the improvement over Table III which use traditional insulin-glucose model for predictions during and after physical activity. A few of the 15 subjects had CGM dropouts during the exercise periods that had a direct effect on the results. Data was interpolated in these cases which may have introduced an additional error in predictions. Subject 2 exhibits such a phenomena. The new exercise model can also be used in glucose control to provide an extra safety due to its accurate predictions. Slow glucose sensor response at the beginning of the exercise and rapid change afterwards may be due to sensor delay or slow peripheral circulation of blood compared to central blood. In either case, activity signals can be used to improve predictions during and after physical activity. As illustrated in Figures 2–5, the model with personalized parameter B can accurately predict glucose trends caused by physical activity.

Predictions of the exercise model are not satisfactory when the activity signal level is low. Since people are not active all the time activity-glucose models are not sufficient for the closed-loop insulin administration. Therefore, for the artificial pancreas design, this model has to run in parallel with an insulin-glucose model and they should be switched depending on the activity level.

This research shows the benefits of activity measurements in improving glucose predictions. Note that physical activity may have additional effects on blood glucose that are more complex. Blood glucose concentration can be a function of active insulin in the body and it can depend on the type of exercise such as aerobic or anaerobic. These issues are beyond the scope of this paper. We also recognize that heart rate monitoring may not be appropriate for everyone with type 1 diabetes, because some individuals with T1DM can develop autonomic dysfunction with resting tachycardia that develops over time, impairing heart rate response to exercise. The objective of the paper is to model the glucose dynamics during physical activity. This study shows the importance of activity sensors in artificial pancreas design and their integration to enhance control performance.

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References

1. The International Diabetes Federation. IDF: Diabetes atlas, sixth edition. 2014. <http://www.idf.org/diabetesatlas>
2. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med.* 1993; 329(14):977–986. [PubMed: 8366922]
3. Sigal RJ, Armstrong MJ, Colby P, Kenny GP, Plotnikoff RC, Reichert SM, Riddell MC. Physical activity and diabetes. *Can J Diabetes.* 2013; 37(Supplement 1):S40–S44. [PubMed: 24070962]
4. Finan DA, Zisser H, Jovanovic L, Bevier WC, Seborg DE. Practical issues in the identification of empirical models from simulated type 1 diabetes data. *Diabetes Technol Ther.* 2007; 9(5):438–450. [PubMed: 17931052]
5. Hinshaw L, Dalla Man C, Nandy DK, Saad A, Bharucha AE, Levine JA, Rizza RA, Basu R, Carter RE, Cobelli C, Kudva YC, Basu A. Diurnal pattern of insulin action in type 1 diabetes: Implications for a closed-loop system. *Diabetes.* Jul.2013 62:2223–2229. [PubMed: 23447123]
6. Turksoy K, Bayrak ES, Quinn L, Littlejohn E, Cinar A. Multivariable adaptive closed-loop control of an artificial pancreas without meal and activity announcement. *Diabetes Technol Ther.* 2013; 15(5):386–400. [PubMed: 23544672]
7. Eren-Oruklu M, Cinar A, Rollins DK, Quinn L. Adaptive system identification for estimating future glucose concentrations and hypoglycemia alarms. *Automatica.* 2012; 48:1892–1897. [PubMed: 22865931]
8. Zecchin C, Facchinetti A, Sparacio G, Dalla Man C, Manohar C, Levine JA, Basu A, Kudva YC, Cobelli C. Physical activity measured by physical activity monitoring system correlates with glucose trends reconstructed from continuous glucose monitoring. *Diabetes Technol Ther.* 2013; 15(10):1–9. [PubMed: 23297669]

9. Dasanayake IS, Bevier WC, Castorino K, Pinsky JE, Seborg DE, Doyle FJ III, Dassau E. Early detection of physical activity for people with type 1 diabetes mellitus. *J Diabetes Sci Technol*. 2015
10. Dalla Man C, Breton MD, Cobelli C. Physical activity into the meal glucose-insulin model of type 1 diabetes: In silico studies. *J Diabetes Sci Technol*. 2009; 3:56–67. [PubMed: 20046650]
11. Walsh, J.; Roberts, R. *Pumping Insulin*. Torrey Pines Press; 2006.
12. Finan DA, Palerm CC, Doyle FJ III, Zisser H, Jovanovic L, Bevier WC, Seborg DE. Identification of empirical dynamic models from type 1 diabetes subject data. *Proc American Control Conf*. Jun. 2008 :2099–2104.
13. van Heusden K, Dassau E, Zisser HC, Seborg DE, Doyle FJ III. Control-relevant models for glucose control using a priori patient characteristics. *IEEE Trans Biomed Eng*. 2012; 59(7):1839–1849. [PubMed: 22127988]
14. Grosman B, Dassau E, Zisser HC, Jovanovic L, Doyle FJ III. Control-relevant models for glucose control using a priori patient characteristics. *J Diabetes Sci Technol*. 2010; 4(4):961–975. [PubMed: 20663463]
15. Karvonen MJ, Kentala E, Mustala O. The effects of training on heart rate; a longitudinal study. *Ann Med Exp Biol Fenn*. 1957; 35(3):307–315. [PubMed: 13470504]
16. David JV, Convertino VA. A comparison of heart rate methods for predicting endurance training intensity. *Med Sci in Sports Exerc*. 1977; 9:307–315.
17. Lacy SL, Bernstein D. Subspace identification with guaranteed stability using constrained optimization. *IEEE Trans Aut Control*. 2003; 48(7):1259–1263.
18. Grant, M.; Boyd, S. CVX: Matlab software for disciplined convex programming, version 2.1. Mar. 2014 <http://cvxr.com/cvx>
19. Grant, M.; Boyd, S. Graph implementations for nonsmooth convex programs. In: Blondel, V.; Boyd, S.; Kimura, H., editors. *Recent Advances in Learning and Control*. Springer-Verlag Limited; 2008. p. 95–110. ser. *Lecture Notes in Control and Information Sciences*
20. Sturm JF. Using *SeDuMi* 1.02, a MATLAB toolbox for optimization over symmetric cones. *Opt Meth Softw*. 1999; 11(5):625–653.

Fig. 1.
AIC Values for Calibration and Validation Data

Fig. 2. Calibration data and blood glucose predictions for subject 1. The exercise period is shown in gray.

Fig. 3. Validation data and blood glucose predictions for subject 1. The exercise period is shown in gray.

Fig. 4.
Calibration data and blood glucose predictions for subject 8. The exercise period is shown in gray.

Fig. 5.

Validation data and blood glucose predictions for subject 8. The exercise period is shown in gray.

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TABLE I

First element of the control matrix for fifteen subjects

Subject	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
	-1.55	-1.01	-8.78	-1.09	-3.18	-4.91	-7.88	-4.47	-10.3	-3.27	-9.52	-0.93	-9.15	-1.87	-7.44

Average blood glucose prediction error (mg/dl) for calibration (C) and validation (V) data.

TABLE II

Subject	5 min		10 min		15 min		20 min		25 min		30 min	
	C	V	C	V	C	V	C	V	C	V	C	V
1	2.18	1.74	5.35	4.46	8.82	7.71	11.9	10.7	14.6	13.6	16.5	16.4
2	1.64	2.27	3.89	5.36	6.25	8.21	8.45	11.6	10.6	14.3	12.4	17.1
3	1.87	3.28	3.74	8.04	5.07	13.1	6.39	18.5	7.69	23.2	8.74	26.9
4	1.13	1.81	2.63	4.94	4.29	8.23	6.35	11.3	8.24	13.9	10.1	17.1
5	2.24	2.60	3.52	5.90	4.87	8.94	5.72	13.3	6.56	17.5	6.97	21.7
6	2.25	2.23	5.19	5.56	7.46	9.43	9.30	13.8	11.2	18.4	12.9	23.0
7	0.88	2.42	1.70	6.09	2.73	9.67	3.62	13.2	4.47	17.0	5.10	21.1
8	2.79	2.88	5.81	4.76	8.85	7.23	11.5	9.26	13.7	10.7	16.4	11.5
9	1.79	4.92	4.02	10.4	6.16	15.3	7.05	20.5	8.11	26.0	9.76	31.0
10	2.09	4.03	4.90	9.77	7.60	15.0	10.3	18.7	13.4	23.2	16.5	28.9
11	3.53	2.09	7.34	5.19	10.8	8.42	14.5	11.4	16.6	13.6	16.9	15.6
12	1.20	2.07	2.78	5.44	4.70	9.54	6.50	13.7	8.44	18.0	10.6	22.8
13	1.42	1.21	3.74	3.05	6.13	5.19	8.40	7.32	9.84	9.45	10.7	11.9
14	3.50	2.43	7.10	5.74	12.0	9.48	17.7	13.4	22.8	17.4	26.9	21.1
15	3.66	2.74	9.20	7.03	14.9	12.1	18.8	17.4	21.3	23.6	23.8	29.4
Avg.	2.01	2.42	4.43	5.73	9.91	9.22	9.15	12.8	11.1	16.2	12.8	19.7

TABLE III

Average blood glucose prediction error (mg/dl) of the insulin-glucose model given in [13] for the same data set used for the validation of the derived model

Subject	10 min	15 min	20 min	25 min	30 min
1	5.55	9.92	14.9	22.4	31.9
2	8.04	15.4	24.5	37.1	49.6
3	13.6	24.5	38.1	53.7	74.2
4	5.14	10.8	18.5	26.6	36.1
5	9.48	16.4	24.5	34.9	42.3
6	7.08	13.1	20.6	30.9	42.1
7	10.2	17.8	27.9	40.0	53.3
8	10.7	20.2	33.4	47.3	62.7
9	18.5	33.2	51.3	73.9	102
10	16.1	28.5	45.8	66.3	89.8
11	7.29	14.7	24.4	36.1	49.6
12	5.39	11.2	19.2	29.2	40.4
13	4.77	9.24	14.6	22.1	31.1
14	8.68	17.3	28.2	41.0	55.7
15	7.21	13.5	21.1	31.0	41.3
Avg.	8.61	16.0	25.4	37.0	50.2