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Editors
Beben Benyamin and Kasbawati

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Preface: Symposium on Biomathematics 2016

The 4th International Symposium on Biomathematics (SYMOMATH 2016) was successfully held on 7 October - 9 October 2016, at Ibis Hotel, Makassar, Indonesia. SYMOMATH 2016 was jointly organized by Department of Mathematics, Faculty of Mathematics and Natural Sciences, Hasanuddin University (UNHAS), the Indonesian Biomathematical Society (IBMS), and the Indonesian Mathematical Society (IndoMS).

This symposium is multidisciplinary forum for contemporary issues in the various fields of biology, medicine, epidemiology, pharmacology, ecology, biotechnology, bioengineering, environmental sciences, etc. In this symposium researchers, students and industrial practitioners can develop, exchange, collaborate, and apply mathematical, statistical and computational tools for understanding phenomena.

SYMOMATH 2016 has received good feedbacks from mathematicians and participants, local and international, who were interested to participate and present their finding. More than 85 participants attended from all over the countries: Australia, Germany, Portugal, and Indonesia. There were 66 papers presented in this symposium. There were seven invited speakers who delivered a speech with the tittles: Optimal Control in Epidemiology by Prof. Thomas Götz (University of Koblenz-Landau, Germany), How Far the Basic Reproductive Ratio Represents the Intensity of Disease Transmission by Prof. Edy Soewono (Institute Technology Bandung, Indonesia), Power Law Jumps and Power Law Waiting Times, Fractional Calculus and Human Mobility in Epidemiological Systems by Prof. Nico Stollenwerk (Lisbon University, Portugal), The Impact of the Newly Licensed Dengue Vaccine in Endemic Countries by Dr. Maíra Aguiar (Lisbon University, Portugal), Helminth Infections, Socio-economic Status and Allergies in Indonesia by Dr. Firdaus Hamid (Hasanuddin University, Indonesia), Big Data in Genomics of Complex Traits by Dr. Beben Benyamin (The University of Queensland, Australia) and Considering Human Response Behaviour in a Mathematical Model of Wolbachia Infection to Control Dengue Disease by Prof. Asep K. Supriatna (Padjadjaran University, Indonesia). There were 33 papers submitted to AIP Conference Proceedings but after blind review and check plagiarism processes, only 26 papers were selected to be published in this volume.

We would like to thank all presenters and participants for their attention in this symposium. We also would like to thank the plenary speakers, all scientific committee, paper reviewers, all members of committee, UNHAS, IBMS, and IndoMS. Without their supports, this symposium is rather difficult to be held.

Makassar, February 2017

Editors,
Beben Benyamin
Kasbawati

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RESULTS: 21 – 40 of 63 within AIP Conference Proceedings

Follow res

ARTICLE TYPE

- Research Article 61
- Introduction 2

PUBLICATION DATE

2016 2019

TOPICS

- Mathematical modeling 20
- Diseases and conditions 18
- Computer simulation 11
- Regression analysis 7
- Insects 6

MORE (21)

AUTHOR

- Nuraini, Nuning 8
- Bustamam, Alhadi 6
- Nuraini, N 6
- Aldila, D 4
- Soewono, E 4

MORE (95)

ARTICLES (63)

Refine Search

SORT: Re

Mar 27, 2017 . 1 Citations

Mathematical modeling of transmission co-infection tubercul HIV community

V. Lusiana, *P. S. Putra*, *N. Nuraini* and *E. Soewono*

AIP Conference Proceedings **1825**, 020012 (2017); https://doi.org/10.1063/1.4978981

Mar 27, 2017

Multiresponse semiparametric regression for modelling the ef regional socio-economic variables on the use of information technology

Wahyu Wibowo, *Chatrien Wene*, *I. Nyoman Budiantara* and *Erma Oktania Permatasari*

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Mar 27, 2017 . 1 Citations

Implementation of spectral clustering with partitioning aroun medoids (PAM) algorithm on microarray data of carcinoma

Rosalia D. Cahyaningrum, *Alhadi Bustamam* and *Titin Siswantining*

AIP Conference Proceedings **1825**, 020007 (2017); https://doi.org/10.1063/1.4978976

Mar 27, 2017

Artificial immune system for diabetes meal plans optimizatior

K. R. Prilianti, *P. B. Callista* and *H. Setiawan*

AIP Conference Proceedings **1825**, 020017 (2017); https://doi.org/10.1063/1.4978986

Mar 27, 2017 . 3 Citations

Optimal harvesting policy of predator-prey model with free fis and reserve zones

Syamsuddin Toaha and Rustam

AIP Conference Proceedings **1825**, 020023 (2017); https://doi.org/10.1063/1.4978992

Mar 27, 2017 . 5 Citations

Assessing the effect of extrinsic incubation period (EIP) prolor in controlling dengue transmission with wolbachia-infected mosquito intervention

Y. E. Putri, S. Rozi, H. Tasman and D. Aldila

AIP Conference Proceedings **1825**, 020019 (2017); https://doi.org/10.1063/1.4978988

Mar 27, 2017

Gross regional domestic product estimation: Application of tw unbalanced panel data models to economic growth in East Nu Tenggara province

Wahyu Wibowo, Elisabeth B. Sinu and Setiawan

AIP Conference Proceedings **1825**, 020026 (2017); https://doi.org/10.1063/1.4978995

Mar 22, 2019

Mathematical model of dengue transmission based on daily d Bandung

Muhammad Fakhruddin, Nuning Nuraini and Sapto Wahyu Indratno

AIP Conference Proceedings **2084**, 020013 (2019); https://doi.org/10.1063/1.5094277

Mar 22, 2019

Protein sequence analysis of the Zika virus and the dengue vir using Smith Waterman algorithm

Mohammad Syaiful Pradana and Siti Amiroch

AIP Conference Proceedings **2084**, 020011 (2019); https://doi.org/10.1063/1.5094275

Apr 6, 2016

Preface: Symposium on Biomathematics 2015

AIP Conference Proceedings **1723**, 010001 (2016); https://doi.org/10.1063/1.4945055

Apr 6, 2016 . 1 Citations

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S. Viridi and N. Nuraini

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Apr 6, 2016

Coefficient of restitution dependence of intruder rise time in t dimensional Brazil-nut effect

T. Kesuma, D. P. Purwa Aji, S. Viridi and Suprijadi

AIP Conference Proceedings **1723**, 030014 (2016); https://doi.org/10.1063/1.4945072

Mar 6, 2018

A model of immunomodulatory for dengue infection mm

Annisa Zulfa, Dewi Handayani and Nuning Nuraini

AIP Conference Proceedings **1937**, 020024 (2018); https://doi.org/10.1063/1.5026096

Apr 6, 2016 . 2 Citations

Nonstandard finite difference scheme for SIRS epidemic mod disease-related death

Z. Fitriah and A. Suryanto

AIP Conference Proceedings **1723**, 030009 (2016); https://doi.org/10.1063/1.4945067

Apr 6, 2016

A modelling on estimation of the carbon dioxide emission fror vehicles using logistic equation

E. W. Chandra, A. Andry, F. Afra and N. Sumarti

AIP Conference Proceedings **1723**, 030005 (2016); https://doi.org/10.1063/1.4945063

Apr 6, 2016 . 1 Citations

Convergence analysis of particle swarm optimization (PSO) m on the with-in host dengue infection treatment model

D. Handayani, N. Nuraini, O. Tse, R. Saragih and J. Naiborhu

AIP Conference Proceedings **1723**, 030013 (2016); https://doi.org/10.1063/1.4945071

Apr 6, 2016

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Tasmi, D. Aldila, E. Soewono and N. Nuraini

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Apr 6, 2016 . 1 Citations

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Susila Bahri

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Apr 6, 2016 . 1 Citations

Model of two infectious diseases in nettle caterpillar populatic

Artificial Immune System for Diabetes Meal Plans Optimization

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Abstract. Type 2 diabetes mellitus is a disease that occurs because the body lacks of insulin or the insulin produced by the pancreas cannot work effectively such that the glucose level in the blood cannot well controlled. One of the most common causes of diabetes mellitus type 2 is obesity, therefore this disease can be controlled with the appropriate diet regarding to the daily calorie requirement. Hence, the level of blood glucose is maintained. Unfortunately, because the lack of proper diet education and facility, many people cannot work on proper daily healthy diet by their own. In this research Artificial Immune System algorithm was applied to build a model that help diabetes mellitus patient arrange their meal plans. The model can calculate the amount of daily calorie needed and arrange the appropriate daily meal plans based on it. The meal plans vary according to the patient calorie needs. The required input data are age, gender, weight, height, and type of patient daily main activity. The experiments show that this model has a good result. The result is already approaching the patients' daily calorie need, i.e. 97.6% (actual need is not less than 80% and not greater than 100%). Carbohydrate of the meal plan is 55-57% (actual need is not less than 45% and not greater than 60%) whereas the protein approximate 15-18% (actual need is not less than 15% and not greater than 20%) and fat of approximate 22-24% (actual need is not less than 20% and not greater than 25%).

INTRODUCTION

Diabetes mellitus is one of chronical disease that needs long term medical treatment. Factors that stimulate the occurrence of this disease are obesity, high level of triglycerides in blood, genetic susceptibility, smoking habit and hormonal abnormality. Among those factors, the most common cause is obesity which related to improper diet. Obesity occurs when a person has accumulated so much body fat. Excessive fat in blood could reduce sensitivity of the insulin (the hormone which control blood glucose level) and leads to a condition in which cells fail to respond to insulin properly. Commonly, thus condition is recognizes as type 2 diabetes mellitus. Therefore, a tight diet control is the main method for the patient to deal with type 2 diabetes mellitus. Diet control for Type 2 diabetes mellitus is focused on sugar content distribution on daily meal such that total calorie consumption do not exceed the patients' calorie need. Hence, blood glucose level is maintained below the normal treshold.

Meal plan arrangement for type 2 diabetes mellitus is not an easy task since food nutrition content and daily calorie need is not a common knowledge. Moreover, consultation fee for a nutritionist is not cheap either. Those are some obstacle that prevent type 2 diabetes mellitus patient from having a good treatment at home. Some researchers had been try to develop an automatic system for meal plan arrangement using various techniques. For example ant colony optimization algorithm [1], bayesian optimization algorithm [2] and simplex algorithm [3]. Unfortunately, those system is not provide patient with an "easy to do" menu. It just suggest the raw material rather than a food recipe. Patient still need to find out how to mix those raw material into delicious food. Another problem is the total running time needed. Using previous method the running time can not support dynamic and online system. Therefore, the system is deployed in offline mode which is not practical for nowadays used in internet of thing era.

In this research, a technique based on human imune system concept was developed to modeled the meal plan arrangement for type 2 diabetes mellitus and speed up the running time. Using this model, the patient will automatically get personal menu suggestion that match their nutrition daily need. As an additional, the model can

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also generate several similar menu to provide alternative for the patient. The model was deployed in web-based application to provide ease of access.

MATERIALS AND METHOD

As much as 200 Indonesian meals recipes were collected from various sources (internet, recipe books, private collection) to be saved in the database. Those recipes are covers meals for breakfast, lunch, dinner and snack time. The main requirement for the recipes to be fit on the model is it must inform the serving size and the size of each ingredient being used. In the preprocessing step, the sizes were transformed into calorie (in cal) using food catalog like the USDA National Nutrient Database.

Type 2 Diabetes Mellitus Meal Plans

In fact, there is no significant difference on meal arrangement between people with diabetes and normal people. Both of them can eat the same foods, but people with diabetes should concern on the daily total amount of the nutritional content on their meal. It must must be ensure that the daily total calorie intake is match the total calorie need in a day. The total calorie need is depends on gender, daily activity, weight, height, age and other conditions, such as being pregnant [4]. First, the ideal weight should be determines using Eq. 1 and Eq. 2, followed by basal calorie calculation using Eq. 3 and Eq. 4.

$$Female\ Ideal\ Weight = \begin{cases} Height - 100, & Height < 160\ cm \\ (Height - 100).90\%, & Height \geq 150\ cm \end{cases} \tag{1}$$

$$Male\ Ideal\ Weight = \begin{cases} Height - 100, & Height < 160\ cm \\ (Height - 100).90\%, & Height \geq 160\ cm \end{cases} \tag{2}$$

$$Female\ Basal\ Calorie = \begin{cases} -5\%.Ideal\ Weight.25, & Age\ \geq 40\ year \\ -10\%.Ideal\ Weight.25, & Age \geq 60\ year \\ -20\%.Ideal\ Weight.25, & Age \geq 70\ year \end{cases} \tag{3}$$

$$Male\ Basal\ Calorie = \begin{cases} -5\%.Ideal\ Weight.30, & Age\ \geq 40\ year \\ -10\%.Ideal\ Weight.30, & Age \geq 60\ year \\ -20\%.Ideal\ Weight.20, & Age \geq 70\ year \end{cases} \tag{4}$$

The daily total calorie need is then calculates regarding to the type of the daily activity (rest, light, moderate, heavy or very heavy) and weight category (under weight or overweight) using Eq. 5 and Eq. 6 consecutively. Total calorie intake for one day should not exceed the daily total calorie need. Another requirement is related to the nutrition distribution. The recommended distribution for type 2 diabetes mellitus patient are 45% up to 60% carbohydrate, 15% up to 20% protein and 20% up to 25% of fat. Moreover, it is highly recommend that the daily calorie intake is distributes as follows, 20% from breakfast, 30% from lunch, 30% from dinner and 25% from snack time,

$$Calorie\ Need\ = \begin{cases} +10\%.Basal\ Calorie, & Activity = Rest \\ +20\%.Basal\ Calorie, & Activity = Light \\ +30\%.Basal\ Calorie, & Activity = Moderate \\ +40\%.Basal\ Calorie, & Activity = Heavy \\ +50\%.Basal\ Calorie, & Activity = Very\ Heavy \end{cases} \tag{5}$$

$$Calorie\ Need = \begin{cases} -20\%.Basal\ Calorie, & Weight < 110\%.Ideal\ Weight \\ +20\%.Basal\ Calorie, & Weight \geq 110\%.Ideal\ Weight \end{cases} \tag{6}$$

Artificial Immune System

Artificial immune system (AIS) is one among the methods in the field of biologically-inspired computing to solve computational problems. It concerns on abstracting the immune system mechanism of the vertebrate to computational system. Generally, immune system refers to the defence machanism agains pathogens using an agent called antibodies. These antibodies are generated specific to the pathogen agent called antigen, the purpose is to remove the antigen before it spread and cause major damage. B-cell and T-cell are two types of lymphocyte (white blood cell) which is responsible for the production of antibodies.

Various optimization problems have been solved using this approach [5]. Some techniques which is used in this system are clonal selection algorithm, negative selection algorithm, immune network algorithm and dendritic cell algorithm. Clonal selection algorithms are the most common technique to solve optimization problem, part of them similar to parallel hill climbing and the genetic algorithm but left out the recombination operator [6-7]. It is mimicking the theory of clonal selection of acquired immunity whereas B-cell and T-cell is in the state of affinity maturation (the condition when both cells improve their response to antigens over time). Selection procedure is inspired by the affinity of antigen-antibody interactions, only cells that successfully recognize the antigen will proliferate, thus being selected against cells that do not. Cell division is inspiring the reproduction procedure, and somatic hypermutation is inspiring the variation. Hence, the clonal selection theory's main features are: (1). New cells are duplicates of their wellspring (clone) subjected to a mutation mechanism with high rates (somatic hypermutation); (2). Displacement of newly differentiated lymphocytes carrying self-reactive receptors; (3). Proliferation and differentiation on contact of mature cells with antigens.

There are four basic step to implement basic AIS i.e. encoding, calculating the similarity, selection and mutation. But the first task is defining the antigen and antibody data structure. An antigen is the solution (target) and antibodies are the rest of the data. It is possible to maintain more than one antigen at a time. The antibodies usually present in a large number simultaneously. The representation of antigens and antibodies should be exactly the same, therefore they should be encoded in the same way. Generally, the most obvious representation is a string of numbers or features, where the length is the number of variables, the position is the variable identifier and the value (could be binary or real) of the variable.

Model Building

The most important step during model building is defining the representation of antigen and antibody. It could be represents as vectors or matrices. Table 1 depicts the general concept which is used to create the antibodydies in this research. The meal time divided into 5 categories, i.e. breakfast, snack 1, lunch, snack 2, and dinner. Meanwhile, the meal recipes divided into 7 categories, i.e. rice, meat/poultry/fish, vegetables, bread/cereal, milk, fruits and cake/cookies.

TABLE 1. The arrangement of meal recipe category for each meal time

Meal Time	**Recipe Category**						
	Rice	Meat/ Poultry/ Fish	Vegetables	Bread/ Cereal	Milk	Fruits	Cake/ Cookies
	R	MPV	V	BC	M	F	CC
Breakfast	√	√	√	√	√	x	x
Snack 1	x	X	x	x	x	√	√
Lunch	√	√	√	x	x	x	x
Snack 2	x	X	x	x	x	√	√
Dinner	√	√	√	x	√	x	x

The cells with cross symbol (x) indicate that a particular meal time will not use the meal recipes category and the cells with check symbol (√) indicate that a particular meal time will use the meal recipes category in the coresponding column. As an example, for lunch time, the meal recipes from category bread/cereal, milk, fruits and cake/cookies will not be chosen from the database and in the other hand the category rice, meat/poultry/fish and vegetables will be chose. This basic rule is based on the regular Indonesian meal arrangement. But, it could be modified to adjust the eating habit for other culture. This rule was then used to pick up the recipes for the antibody. Each antibody will bring information about the recipe code used in the database and then retrives the coresponding total calorie. The code was created based on the arrangement as shown in Table 2. It consist of 4 digit, the first digit represnt the recipe's category and the other 3 digits represent the recipe identity number on database.

TABLE 2. Code arrangement for each category of recipe

Breakfast			**Snack 1**		**Lunch**			**Snack 2**		**Dinner**		
R	MPV	V	F	CC	R	MPV	V	F	CC	R	MPV	V
1xxx	2xxx	3xxx	6xxx	7xxx	1xxx	2xxx	3xxx	6xxx	7xxx	1xxx	2xxx	3xxx

Figure. 1 is the examples of vectors in a population which are created based on rule on Table 1 and code arrangement on Table 2. Each population contains 20 antibodies, one antibody represent as a vector which each cell on it contain a code which is refers to the particular recipe. Those codes are used to retrive the calorie amount of each coresponding recipe. For each vector, the calculation is done to obtain the total calorie from the recipes and its ditribution for each meal time.

Antibody 1 = [1001, 2005, 3023, 6012, 7001, 1002, 2016, 3003, 6008, 7025, 1004, 2003, 3012]
Antibody 2 = [1004, 2015, 3031, 6002, 7021, 1015, 2017, 3015, 6002, 7005, 1001, 2013, 3011]
Antibody 3 = [1001, 2012, 3001, 6010, 7013, 1013, 2015, 3011, 6009, 7014, 1002, 2017, 3021]

: : : : : : : : : : : : : :

Antibody 20 = [1003, 2022, 3004, 6017, 7011, 1003, 2003, 3017, 6011, 7019, 1009, 2027, 3022]

FIGURE 1. Vector representation of antibodies

The affinity measurement between antibody and antigen is conducted using Eq. 7 and Eq. 8, c_{ag} is carbohydrate of the antigen, c_{ab} is carbohydrate of the antibody, p_{ag} is protein of the antigen, p_{ab} is protein of the antibody, f_{ag} is fat of the antigen, f_{ab} is fat of the antibody, cal_{ag} is fat of the antigen and cal_{ab} is fat of the antibody.

$$affinity = \frac{1}{fitness} \quad (7)$$

$$fitness = (\left(c_{ag} - c_{ab}\right) + \left(p_{ag} - p_{ab}\right) + (f_{ag} - f_{ab})) * 0.3) \ + (\left(cal_{ag} - cal_{ab}\right) * 0.7) \quad (8)$$

Using Eq. 8 the priority of the requirement condition is set up. In this research, the total calorie fulfillment is weighted 70% and the calorie distribution is weighted 30%. These weights could be adjusted as the requirement of the system change. Hence, the artificial immune system procedure is apply [8,9]. Figure 2 decpict the flowchart of the procedure.

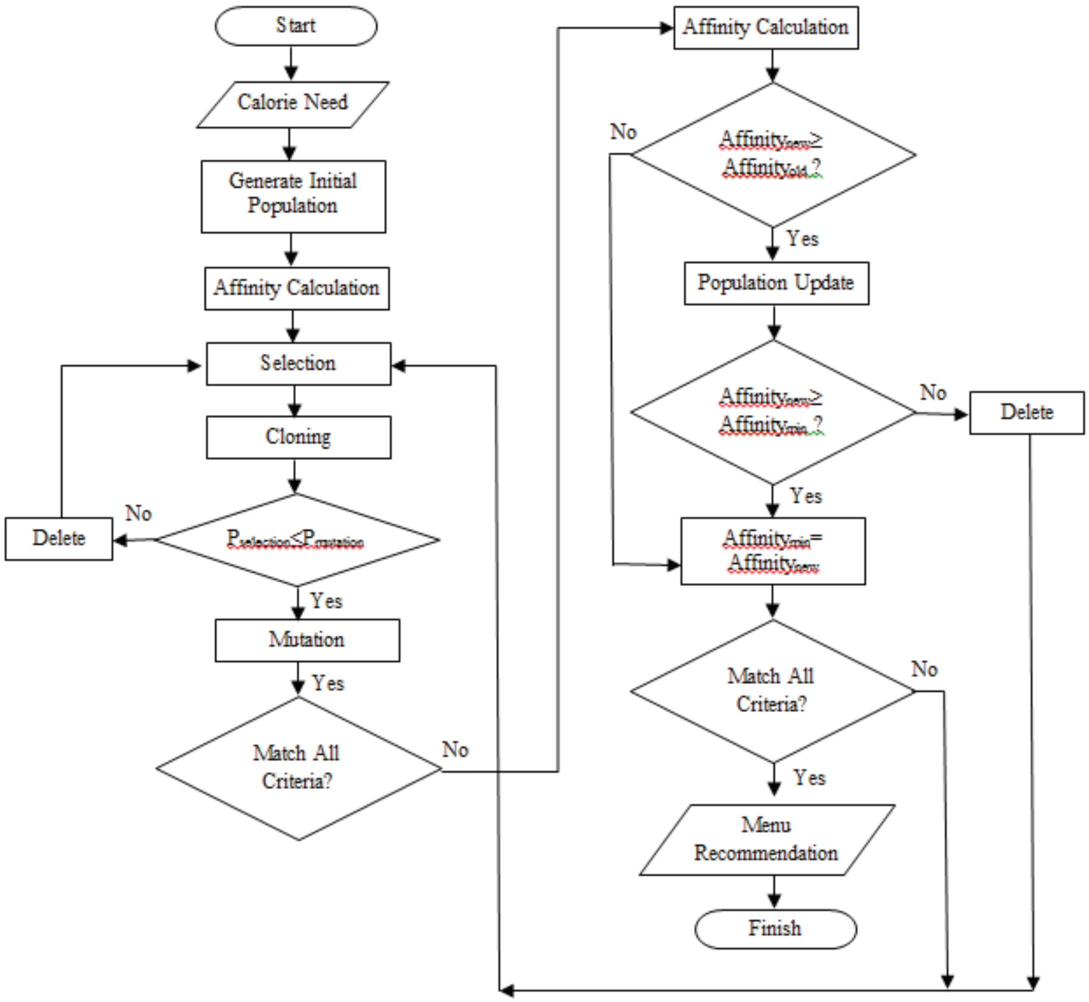

FIGURE 2. Flowchart of the system

Selection of the antibody is done using a selection probability (Eq. 9). Antibodies with high selection probability will be cloned using Eq. 10. Therefore, as the selection probability increase, the number of clone is increase as well. This mechanism ensures that only the best antibody will remain until the end of the procedure.

$$selection\ probability_{ab} = \frac{affinity_{ab}}{\sum affinity_{ab}} \tag{9}$$

$$N_{clone\_ab} = N_{pop}.selection\ probability_{ab} \tag{10}$$

In order to create the positive variation of the antibody, mutation process is applies to the selected antibody. The mutation probability is calculates using Eq. 11.

$$mutation\ probability_{ab} = 1 - selection\ probability_{ab} \tag{11}$$

The two values (selection probability and mutation probability) are then compared, if selection probability is less than mutation probability the antibody will mutate. Mutation is applies by randomly pick up one recipe from the antibody and switch it with other recipe in the same category. The mutation result then evaluate whether it could be remain on the population or should be discarded. The process will be run over and over again until at least 80% of the population contains exactly the same antibodies and the recommendation is determines from those antibodies.

RESULT AND DISCUSSION

Table 3 represents an example of the menu which is recommended by the system for overweight patient. It could be seen that the recommended menu is “ready to use”, it is equipped with the exact serving size that help the patient consume the meal in right dose. Detail of the calorie amount is also provided such that quality of the menu could be easily evaluated.

TABLE 3. Example of the recommended menu.

Meal Time	Recipe	Serving Size		Calorie (cal)	Carbohydrate (cal)	Protein (cal)	Fat (cal)
		Portion	gram				
Breakfast	Raisins Cake	0.5	15	49	32	8	9
Breakfast	Yoghurt	1	240	136	80	56	0
Snack 1	White Bread	0.5	70	194	160	16	18
Snack 1	Bake Peanut	1	15	100	16	12	72
Lunch	Fried Rice	0.5	75	129	64	20	45
Lunch	Bake Catfish	0.5	50	94	0	40	54
Lunch	Butter Corn	0.5	50	61	44	8	9
Snack 2	Kemang	0.5	105	48	48	0	0
Snack 2	Macademia Nut	1	13	57	8	40	9
Dinner	Chicken Steam Rice	1	150	258	128	40	90
Dinner	Vegetable salad	1	100	20	12	8	0
Dinner	Milk	0.5	100	90	20	16	54
	Total			**1236**	**612**	**264**	**360**

Moreover, a web based interface was developed to provide patient with an interactive experience. Patient could get the detail information by clicking the recipe of interest. The information contains “how to make” and also pictures of the meal. It also provides information regarding the quality of the recommended menu, whether it is good or poor to fulfill the patient’s calorie need. If its quality is poor, patient could reruns the system to get new recommendation. Therefore, patient could decide by themselves which menu should be retains and which menu should be discard. Figure 3 depict example of the system’s web interface screenshot.

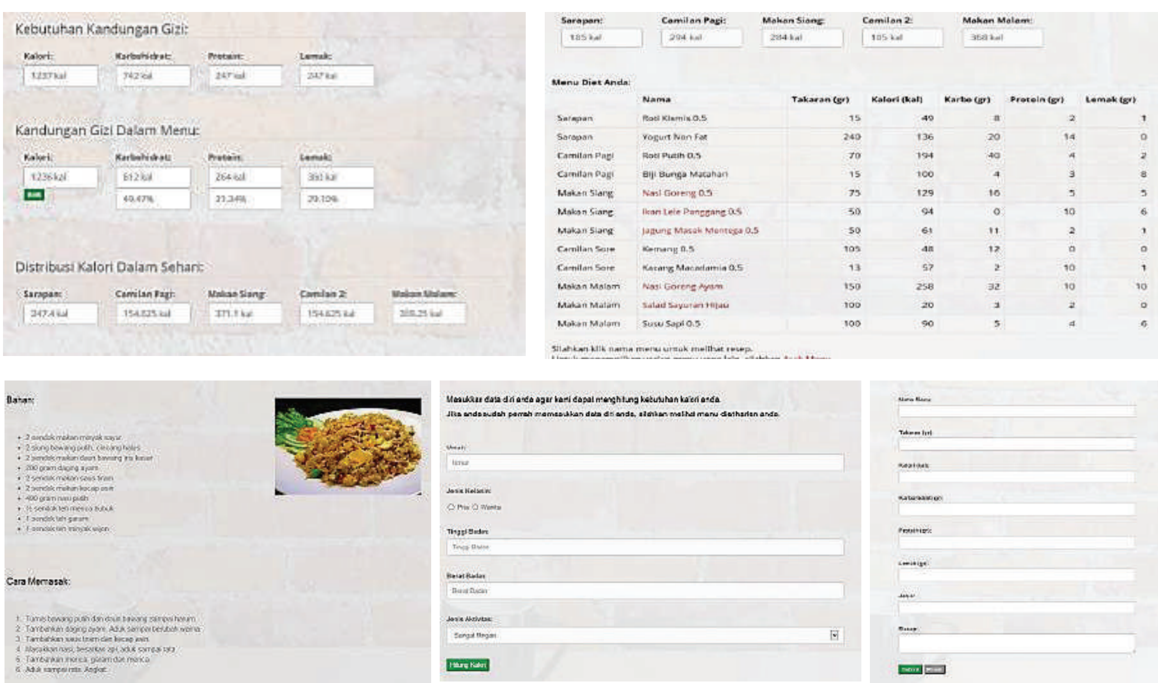

FIGURE 3. Screenshot of the system’s web based interface.

In order to test the system's performance, an experiment was conduct using 30 patients with different body mass profile i.e. overweight, ideal and underweight. Table 4 present the summary of the system performance to fulfill the patient's daily calorie need. Overall, the system performance is satisfying. It is shown that the systems tend to recommend recipes with total calorie less than the patient's calorie need. In the case of diabetes, the total calorie intake should not exceed the total calorie need. Therefore, the system tendency would not bring negative effect for the patient. Moreover the average deficiency is only 2.4%, this number far below the maximum calorie intake deficiency treshold which is 20%. The average running time is also acceptable to be deployed in the web environment. However, the summary also reveals that for underweight cases the system tend to less accurate compare to the other two. Adjustment should be made to the serving unit size of the recipe. It seems that the serving unit size of the common recipe is more suitable to fulfill the calorie need for overweight and ideal cases. The recipe database should be enriched with the ability to automatically create the variation of the smaller serving unit size.

TABLE 4. Summary of the system's performance on fulfillment of the daily calorie need.

	Calorie Need (cal)	**Calorie from The Recommended Recipe (cal)**	**Difference (cal)**	**Iteration**	**Running Time (s)**
Overweight	1573	1537	36	370	6.674
Ideal	1880	1850	30	408	3.394
Underweight	2188	2117	71	677	5.208

Figure 4 depict the system's performance on the distribution of fat, protein and carbohydrate which is compared to the minimum and maximum healthy diet requirement. It is shown that the system successfully meet the requirement. The overall fat, protein and carbohydrate distribution for three categories of patient's body mass is reasonably lies between minimum and maximum amount. A little imperfection was happened for fat distribution, the system tend to recommend recipe which is contain fat at merely maximum allowable amount.

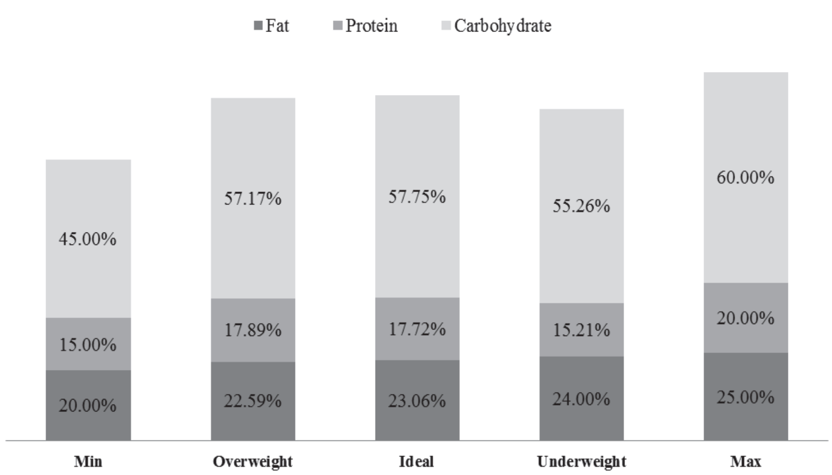

FIGURE 4. System's performance on main nutrition distribution

Figure 5 depicts the system's performance to distribute the calorie for each meal time. It compares the required calorie distribution to the calorie distribution on recipe which is recommended by the system. It is shown that in general, the system could reasonably match the requirement, indicate that the system could organize the recipe regarding the meal time calorie suggestion. However, the figure also reveals that for snack 1 and snack 2 the system tends to recommend recipe with the total calorie above the requirement. Meanwhile, for lunch time the system tends to recommend recipe with the total calorie below the requirement. Adjustment should be made on the database that handles the fruits and cake/cookies category. The serving unit size should be reviewed for those categories. But, since the daily total calorie from the recipe could well match the daily total calorie need, this tendency will not bring major problem for the patient.

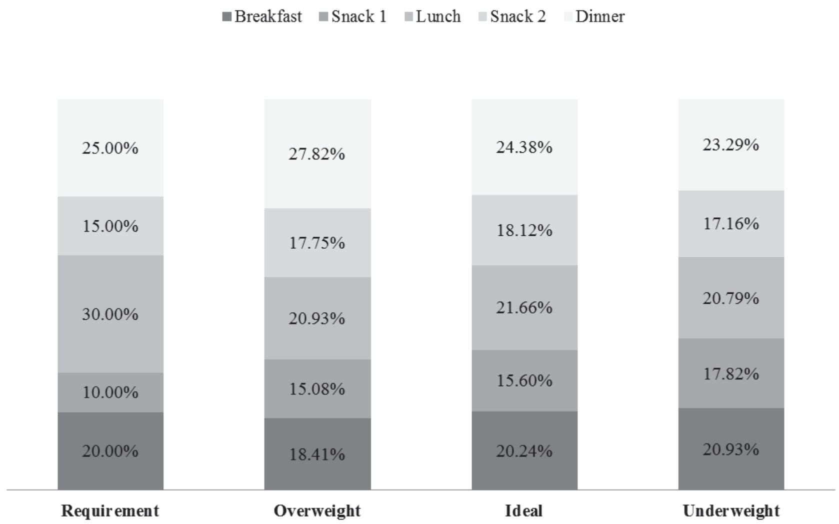

FIGURE 5. System's performance on meal time's calorie distribution

CONCLUSION

The evaluation of the artificial immune system model for diabetes meal plan optimization in this work shows very promising result. Accuracy of daily calorie fulfillment from the recommended menu reach 97.6% and its main nutrition (carbohydrate, protein and fat) distribution lies between the ideal thresholds. Distribution of the calorie regarding the meal time is reasonably appropriate as well. Running time test of the web based environment system was also indicates that the web application could run well in the World Wide Web. However, a little adjustment is still need to be done on the recipe database. It would be much better if the databases could automatically adjust the serving size to the exact amount needed by the patient such that it could be well adapt to the patient body mass category. Another artificial intelligence technique e.g. fuzzy logic could be applies for this matter. Using such hybrid technique will increase the accuracy of the system [10-11].

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