Modeling Diseases with Stream X machine

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***Abstract*— At present the world is moving towards alternative medicine and behavioural alteration for treating, managing and preventing chronical diseases. With the individuality of the human beings has added more complexity in a domain where very high accuracy is demanded. Formal methods has been proven to be occupied in critical system development. This paper introduces a generic disease model called Stream X-Machine Disease Model (SXMDM) based on X-Machine theory. SXMDM has been developed as a proof of concept that formal methods, especially Stream X-Machines, can be employed to model medical conditions or diseases. We have conducted an experiment on modelling an actual disease using a case study of type 2 diabetes. The results of the experiment have illustrated that the proposed SXMDM is capable of modeling chronic diseases.**

Keywords-component; X-Machine; Stream X-Machine; Formal Methods; Chromical Diseases; Type II Diabetes

I. INTRODUCTION

At present the world is moving towards preventive medicine and lifestyle intervention in order to have a healthy life. Food that we eat has a significant impact on our medical conditions and on our health in general [1]. Studies has shown that there is a direct relationship between the dietary and lifestyle habits and health [2]. Non-communicable, nutritional related diseases are common, costly yet preventable but being significantly neglected subject matter [1]. Even though preventative medicine specially related to managing dietary habits has proven a positive effect on the human wellbeing, physicians are lacking the skills of providing necessary, dietary counselling [3], [4], [5]. With the evolving research and development in the fields of metabolomics, proteomics, and nutrigenomics are shifting the perspective of nutrition and diet management to be considered as medicine and concept of nutrition therapeutics [6] are actively used in experimental patient management.

It is vital that the assessing of long-term and short-term nutritional exposure in managing medical conditions or health in general. In order to assess the nutritional requirement for an individual, we need to consider both the diet (nutritional markers) and biochemical measures of the thy individual to produce a comprehensive assessment of the patient. The ideal tool would be able to comprehensively measure the biomarkers of the individuals (reactions expressions of the genes) against in response to thy exposure to the nutarians [6]. This is a complex and critical analysis where the inaccuracies and/or inefficiencies could leave to significant threat to a human life.

Due to the necessity of very high accuracy in the process of using personalised nutritional treatments, there is a need of tool support where medical professionals can easily access and use in order to treat and manage patients with Chronicle illnesses. At the time of this research, to the best of our knowledge there are very limited recourses/tools available to support multidimensional treatments for patients with chronicle illnesses. This has limited the ability of the healthcare professionals using alternative approaches in providing their service to their patients [7] [8] [9]. This arises the necessity of the tool support in order to practically use this approach in real life.

Human body can be recognized as a complex system, where several constituent systems (e.g., vascular system, digestive system, neural system, etc.) working together towards a common goal [10]. As in any other complex system, there are undesired states that the human body can reach, in general known as diseases. To understand the behavior of these complex system, it is vital that we have the full understanding of the behavior of these components and understand the complex interrelationship among them. Because of these complex relationships, the diseases also have interconnected properties. Due to this the nature of such complex architecture of the human body, it is essential to model the behavior in order to provide tool support.

Formal methods have been used specify many safety critical systems [11] [12] [13]. Hence the criticality and the high demand for accuracy, in this research we have decided to employee formal methods do model the diseases in general, in specific Stream X- Machines (SXMs) as the base component.

This paper is structured as follows; section II illustrates background research and the concepts of SXM. Also, within this section, different formal methods that has been used in modeling and its strengths and weaknesses. Section III we have proposed the disease model using SXM. In Section IV we have discussed the implementation of the disease model. Section V is where a case study is provided to demonstrate how the disease model works using Type II Diabetics case study. Section VI outlines the final discussions about the proposed solution. We have explained the future direction of the research and concluded the paper in section VII.

II. BACKGROUND

A. Finite State Machine, X-Machine and stream X-Machine

X-Machine (XM) [14] is an extension of the finite state machine (FSM), where the FSM is empowered with a data structure and a processing function(s). As explained, XM is very similar to an FSM with the difference of having a data

sent X (type of the machine), where finite set of processing functions Φ operates on the X ($\phi : X \rightarrow X \mid \phi \in \Phi$) and inbuilt memory (M) where thy transitions can alter the memory. In the FSM diagram each transition (arch) is ladled with a processing function of φ ($\varphi \mid \varphi \in \Phi$). Because of the generalization of the type X, X-Machine has proven that it is capability of modelling any type of system accurately and also in a very generic manner where extension and/or modification is possible [15] [16] [17] [18].

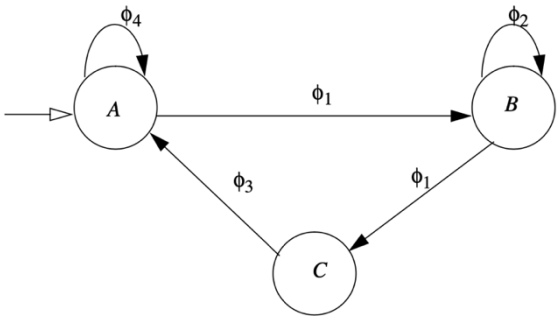

Figure 1: Three state Stream X-Machine [32]

Another class of X-Machine has been introduced to specify and model software namely Stream X-Machines (SXM), which has the ability to define and validate data types and the functionalities of a software systems [17]. Definition of SXM:

$$Z = (\Sigma, \Gamma, Q, M, \Phi, F, q0, m0)$$

Where:

- Σ = input alphabet
- Γ = output alphabet
- Q = finite set of states
- M = memory (possibly infinite)
- Φ = the type of the machine X, where a set of partial functions φ ($\varphi \mid \varphi \in \Phi$) which transforms input and a memory to an output and a possibly to a different memory state. $\phi : \Sigma \times M \rightarrow \Gamma \times M$
- F = Next state partial function which drives the machine state. F: $Q \times \Phi \rightarrow Q$
- q0, m0 = initial state and the initial memory of the machine respectively.

For the above illustrated sxm, the associated FSM is **Az = (Φ, Q, F, q0).** This Az is also known as associated finite state automaton (FA).

B. Disease Modelling and formal methods

Biological systems such as human body consist of tightly connected components (organs) that change their actions and behaviours over the time and their interactions with exposure to external factors (e.g., nutrients, viruses, bacteria). In addressing such challenges, literature reveals that, there are few formal approaches has been occupied namely, Boolean Networks (BN) and its extensions (i.e. Qualitative Networks (QN), Gene Regulatory Networks (GRN) ([19] [20] [21]), Petri Nets (PR), Cellular Automata (CA), population P systems (PPS), etc.

There is an evidence of research that they have used formal methods in order to model biological systems, in specific they have employed Communicating X-Machines in order to model the Biosystems where it has given the ability of representing the interrelationship and the communication aspects of the medical systems [22]. Approximately one third of the world adult population is suffering from Multiple Chronic Conditions (MCCs) [23]. To the best of our knowledge this is the first attempt that formal verification methods has been occupied in order to model a chronic disease.

C. Strengths and weeknesses of existing models

Literature provides evidence of occupying formal methods to model biological systems. However, most of these approaches have not been able to provide the much needed 100% accuracy level in modelling such systems. Hence the medical domain is one of the most critical domains which the cost of a mistake could be a life [24] [25]. In this paper we have considered few approaches and their strengths and weaknesses.

TABLE I. STRENGTHS AND WEAKNESSES OF FORMAL METHODS

Method	Strengths	Weaknesses
BN/QN [19], [20], [21]	Correctly defined binary states.	Due to lack of state space in BN (Active and Inactive), harder to model complex state models such as Biological Systems. Even though, QN discreate variable values, and the dependencies of those values are expressed with algebraical functions instead of Boolean functions, complex relations mapping is not possible.
PR [26], [27]	Has the capability of comprehensive modelling and analysing facility for distributed and concurrent systems.	The ability of providing the concurrency the complexity of the model increases significantly. PR suffers from the inability to test in unbounded places.
CA [28]	Capable of modelling interactive components. CA is a powerful way of defining agent-based system due to the simplicity	CA presents challenges in modelling non-trivial systems due to lack of data representation. CA suffers from state and input symbol explosion

	of following rules and ease of verification	when adding neighbouring agents.
PPS [22]	PPS provides a robust mechanism to introduce new nodes, remove nodes, and change the behaviour of the defined nodes, which helps to map the disease behaviour	PPS lacks the ability to represent internal states and individual behaviour of the nodes

As illustrated above, mathematical models present significant challenges in modelling diseases due to the highly complex interrelationship(s) among the large state space and disease models themselves with other disease models. Due to this highly complex and heavily interconnected model behaviour, most of the mathematical models are being challenged, and/or the models become unmanageably complex [24].

Due to the criticality of the domain in nature, to the best of the authors' knowledge, it is expected that the formal modelling approaches would bring more efficiency and accuracy for disease modelling in general, especially X-Machine models would be more realistic due to their capability in modelling critical systems [29], where interrelationships among the models can be more accurately handled. Therefore, in this research we have selected X-Machines in general to model diseases, particularly Stream X-Machine is used to model type II diabetes to demonstrate the capability of modelling diseases.

III. DISEASE MODELLING USING SXM

A. The packages and the implementation of the disease model

Most of the diseases are having different stages of the disease [30]. It is important to correctly diagnose the disease and its stage before treating the patient. Furthermore, to track and define the negative of positive progression of the disease with the time based on the symptoms and the data.

To the best of our knowledge, this is the first attempt in modeling a chronic disease using Stream X-Machines. In this paper we propose a generic disease model which is capable of representing real world medical diseases using Stream X-Machines to formally model diseases. In this version of the model we have considered that generic disease as the SXM and its variants as the states.

This model can be used by the medicals to:

- Describe diseases and their stages (Demonstration/research purposes for the medical professionals).
- Simulate the progression of the diseases (Positive and negative).
- Determine the stages of the diseases at the time of the patient is being diagnosed.
- Determine the stages with the change of the symptoms.
- Understand the progression of the diseases.
- Monitoring the progression of the patient with past information (Symptoms and data)

General public will benefit from such a tool:

- To understand the behavior of disease.
- To Self-diagnose diseases and take early precautions.

IV. PROPOSED DISEASE MODEL

Class diagram of the proposed SXM disease model is illustrated in the Figure 2. The disease model is illustrated below.

- **XmachineDisease**: this class contains the generic X-Machine model which is implemented iDiseaseType interface.
- **iDiseaseType**: this interface provides the necessary functionalities to describe the type 2 diabetic medical condition.
- **MemoryPair**: this class provides the unit model which holds the memory units.
- **eFunction**: this special class of constant data (enum)class provides all the processing functions that involves in the defining disease type SXM.
- **MemoryTransition**: this class contains the memory transition based on the processing function (eFunction).
- Input: this class provides the input unit which holds in the input sequence of the SXM.
- eDiseaseState: this special class of constant data (enum) provides all the states of the disease.

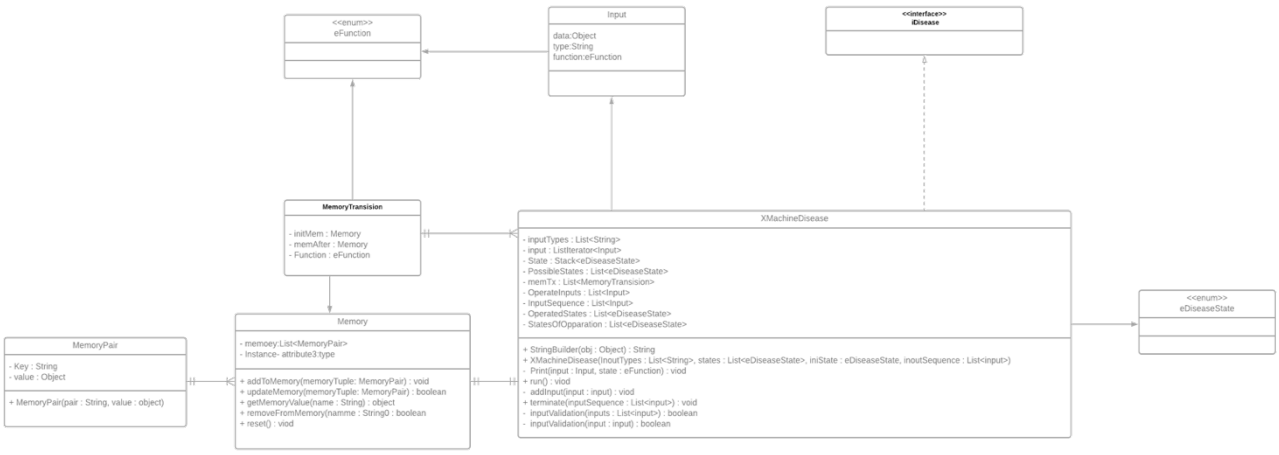

Figure 2: Stream X-Machine Disease Model Class Diagram

B. *Discussion of the Implementation*

Proposed Stream X machine model, mainly consists of two main packages. *Disease.SXM* contains the basic stream x machine model, it's utilities, necessary components of the X-Machine model (memory, defined states, input).

Disease.util contains all the information which is relevant to the disease in discussion. iDisease interface is contained in this package which describes the behaviour of the disease. Based on the disease that we model, meta data such as disease state, processing functions for changing the states will be stored here in form of constants (In this implementation using java we have used enum classes to hold the data)

In this model, we have separated the specific disease 's behaviour from the Stream X-Machine Disease model, so that the Stream X-Machine Disease model can easily adopt any given disease model's behaviour.

V. CASE STUDY

A. *Type II Diabaties Model*

To demonstrate the validity of the Stream X-Machine Disease Model (SXMDM), we consider the implementation of Type II Diabetes Model (TTDM). To test the correctness of the TTDM, we have to adopt the TTDM to SXDM. In our proposed TTDM, we have assumed that the symptom collection is done elsewhere, and the data (Symptom's information) is fed into the model.

B. *Type II Diabaties and Symptoms Evaluation*

There are clearly defined four stages of diabetes namely, pre metabolic syndrome, metabolic syndrome, pre diabetic and type II diabetic. Depending on the time of the diagnosis a patient can be in any of the above mentioned four stages. With the time, a patient can progress his/her diabetic stage positively or negatively.

The initial state of the disease (diabetic) is defined by the number of symptoms that the patient is presenting at the time of the diagnosis [31]. The symptom evaluation criteria to define the stage of the diabetic is as follows.

If a patient is presenting with:

- A waist circumference off:
  - 94 centimetres and above for European men or 90 centimetres an above for South Asian men.
  - 80 centimetres or more for South Asian woman.
- High levels of triglyceride in the blood.
- Low levels of HDL.
- Constant levels of high blood pressure 140 / 90mmHg
- Low levels of insulin response (inability to control blood sugar levels)
- A tendency to develop irritation and swelling off the body tissues in general inflammation.

Based on the above-mentioned criteria, medical professionals evaluate the stage of diabetes. Table 2 illustrates the evaluation criteria of type II diabetes. Based on the illustrated evaluation criteria we have designed the state transition diagram (Figure 3). After acquiring the symptoms, a patient can move to any of the four stages mentioned above. Further with re-evaluation a patient could progress in the diabetic stages. In this paper we demonstrate how Stream X-Machine can be used to model such behaviour of a disease.

TABLE II. DIABETES TYPE EVALUATION BASED ON NUMBER OF SYMPTOMS

Number of Symptoms	Stage of Diabetes
0	Normal
1-2	Pre-Metabolic Syndrome
2-3	Metabolic Syndrome
4-5	Pre-Diabetes
5 or more	Type II Diabetes

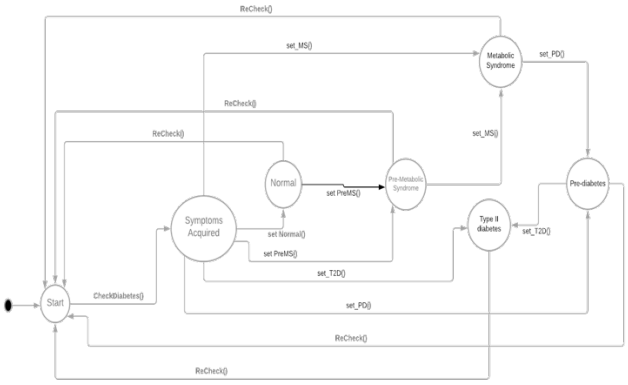

Figure 3: Type II Diabetes State Transition Diagram

The Type II Diabatic Stage Identification can be described as follows: The TTDM is in the ***Start*** State, waiting to process patient's symptoms data. When the patient information is fed in, to start the evaluation process. Then the machine will validate the inputs (Symptom information) and process the data for Type II Diabetic stage evaluation. Assuming that the input data is valid, machine starts the evaluation process. Once the evaluation is completed the machine will determine the Diabatic Stage of the patient. Then machine will wait until recheck occurs to re-evaluate the patient. When the re-evaluation is called, the machine will follow the same process as before.

We consider first stage of the disease as ***Start*** *and* then leads to the state where the symptoms are acquired and validated (Symptoms acquired). Depending on the symptoms that the particular patient presented at the time of the diagnosis, TTDM defines the stage of the disease. Then the TTDM will wait at the particular level till, recall method is called to submit new (updated symptoms), and repeats the same process.

With the above description, SXMDM can be modelled as a SXM with 6 states. The states are as follows:

- Normal: TTDM waits for the recheck data after acquiring the diabetes state.
- Pre-Metabolic Syndrome: TTDM waits for the recheck data after acquiring the diabetes state.
- Metabolic Syndrome: TTDM waits for the recheck data after acquiring the diabetes state.
- Prediabetes
- Type II diabetes: TTDM waits for the recheck data after acquiring the diabetes state.
- Symptoms Acquired: TTDM waits for identifying the diabetes stage.
- Start **(initial state):** TTDM waits for the patient data.

The memory of the TTDM consists of one element with accordance to our implementation.

- Diabetes: a data object of the disease which contains all the necessary to evaluate a patient's diabetic stage.

In the TTDM, we have identified that there are seven functions but drives the model and one internal function.

- set_PreMS(Diabetes diabetes)
- set_MS(Diabetes diabetes)
- set_PD(Diabetes diabetes)
- set_Normal(Diabetes diabetes)
- set_T2D (Diabetes diabetes)
- checkDiabetes(Diabetes diabetes)
- get CurrantState()
- reCheck(Diabetes diabetes)

C. Demostration of the TTDM

For demonstration purposes let us assume that a patient is presenting with high levels of triglyceride in the blood, low levels of HDL, consistent high blood pressure, a waist circumference in normal range and no complaints about body inflammation and high level of insulin response. TTDM initially will be in the *Start* state. When the symptoms are given, TTDM invokes checkDiabetes(Diabetes diabetes) processing function, which updates the memory of Diabetes with the data object. Then the TTDM evaluates the Diabetes data object and analyse the number of symptoms present, against the evaluation criteria. Then amends the input sequence with the relevant processing function. In this scenario the patient is presenting with four positive symptoms and two negative symptoms. Therefore, the TTDM will evaluates the symptoms and decides the next state as ***Metabolic Syndrome***. Then the set_MS(Diabetes diabetes) processing function will be called and updates the Diabetic memory with the identified diabetes stage. Then waits until reCheck(Diabetes diabetes) processing function is called to re-evaluate the condition with new data. State transition with the given inputs is illustrated in Figure 4.

Figure 4: State Transitions of Type Two Diabetes from TTDM

According to the above given scenario the TTDM should work properly by consuming the diabetes date object and setting the TTDM state as Metabolic Syndrome. Furthermore, to the above scenario we have given a second diabetes data object with the reCheck(Diabetes diabetes) processing function, which has all symptoms are positive for type II diabetes, to demonstrate the transitions. The sequences of input and output are illustrated respectively in Figure 5 and Figure 6.

```
// First set of parameters

//Set Triglyceride Levels
Triglyceride triglyceride_1 = new Triglyceride(eLevels.HIGH);

//Set HDL Levels
HDL hdl_1 = new HDL(eLevels.HIGH);

//Set Waist Circumference
WaistCircumference waistCircumference_1 = new WaistCircumference(eGender.Male, 100, eLevels.HIGH);

//Set Blood Preasure Levels
BP bp = new BP(eLevels.HIGH);

//Set Tissue Condition Status
TissueCondition tissueCondition_1 = new TissueCondition(true, true);

//Set Waist BloodGloucose Levels
BloodGloucose bloodGloucose_1 = new BloodGloucose(0, eLevels.HIGH);

//Set undefiened Stage
eDiabaticState diabaticState_1 = null;

//Creates Diabetic Data Object
Diabetes diabetes_1 = new Diabetes(triglyceride_1, hdl_1, waistCircumference_1, bp, tissueCondition_1, bloodGloucose_1, diabaticState_1);

// Second set of parameters

 //Set Triglyceride Levels
Triglyceride triglyceride_2 = new Triglyceride(eLevels.LOW);

//Set HDL Levels
HDL hdl_2 = new HDL(eLevels.LOW);

//Set Waist Circumference
WaistCircumference waistCircumference_2 = new WaistCircumference(eGender.Male, 100, eLevels.LOW);

//Set Tissue Condition Status
TissueCondition tissueCondition_2 = new TissueCondition(true, true);

//Set Waist BloodGloucose Levels
BloodGloucose bloodGloucose_2 = new BloodGloucose(0, eLevels.HIGH);

//Set undefiened Stage
eDiabaticState diabaticState_2 = null;

Diabetes diabetes_2 = new Diabetes(triglyceride_2, hdl_2, waistCircumference_2, bp, tissueCondition_2, bloodGloucose_2, diabaticState_2);

inputStream.add(new Input(eFunction.CHECK_DIABETES, diabetes_1, diabetes_1.getClass().getSimpleName()));
inputStream.add(new Input(eFunction.RECHECK, diabetes_2, diabetes_1.getClass().getSimpleName()));
```

Figure 5: Input Sequence of the TTDM

VI. FINAL DISCUSSION

Within the scope of this research, TTDM has provided the capability of modelling type II diabetes and its transformation from pre metabolic syndrome to type II diabetes. SXMDM cannot be recognised as a comprehensive tool for disease modelling since this is lacking a dedicated user interface and the capabilities of modelling substages of diseases. Furthermore, the current version does not have the capability of modelling the interconnectivity of the diseases. However, the TTDM has demonstrated the potential of using SXM in general to model medical diseases which would enable medical professionals and researchers to model diseases accurately and obtain precise data.

Through this research and applying the theory of X-Machines and SXM, we have realised some of the limitations that could affect process modelling diseases. As mentioned earlier, SXMDM does not have the capability of handling inner states. This could potentially be a limitation due to many diseases have internal states (Stages) which would need to be recognised. Further to this, when they are a large number of stages in a disease SXMDM could be really complicated to design and manage.

```
--------------------------------------------------
Start->SymptomsAcquired->MetabolicSyndrome->Start->SymptomsAcquired->TypeIIdiabetes
--------------------------------------------------
```

Figure 6: Sequence of States Visited

As previously discussed, SXMDM can be used by people from different domains (e.g., medical professionals, researchers etc.) but at this particular time, the disease models have to be manually programmed using a preferred programming language (in this instance we have used Java). This is a time-consuming exercise which requires a considerable amount of expertise in programming. This causes a serious limitation on the useability perspective of SXMDM, which could hinder the development of different types of disease models which requires cross domain expertise.

VII. CONCLUSION

With the limitations that has been pointed out in the section VI, we will be keeping improving the current SXMDM. As the way forward initially, we would be looking into other ways of which we can introduce inner states (substages stages) in our SXMDM. This would significantly improve the capabilities of the current version of SXMDM. Furthermore, hence there are complex relationships among the diseases, we would be investigating the possibility of employing communicating stream X-Machines in order to model diseases with their interconnectivity with the other diseases. As discussed in the section II, world is moving towards alternative medicine and behavioural adjustments in order to prevent, mitigate, and manage Chronicle diseases. Our ultimate intention of this research is to come up with a comprehensive tool, which has a suit of disease models which are mapped with their inter-relationships. Such tool will help to the medical industry in managing patients with Chronicle diseases by employing alternative medicine. Furthermore, such tool will reduce the risk of getting complications by administrated medicine.

In conclusion, this paper has presented a novel approach in modelling medical diseases. The presented model is capable of singularly modelling diseases without concerning the inner substages of the disease. although the current version of the disease model inherits number of limitations as discussed in the section VII, SXMDM presents a novel approach in disease modelling domain. As main researchers in this project, we consider this is one of the saucerful milestones of our research. We will be conducting further research in order to improve the disease modelling and to come up with a tool support. Through this we firmly believe that this modelling tool will benefit in many ways in medical domain and will change the perspective of administrating patients with chronical illnesses.

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