NEW APPROACHES OF COMBINED MODELLING AND SIMULATION IN HEALTH CARE SYSTEMS AND MANAGEMENT

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ABSTRACT
Modelling and Simulation in Health Economy has two main challenges to cope with. First modelling aspects are widely scattered, dealing with problems in economy, epidemics, medical aspects and more. Second the identification of models is difficult as data sets are in some ways "hided" in different areas (clinical studies, statistics, economic studies, ..), quality and type of given data sets are various and relationships are complicate to identify. This contribution shows the achievements of the cooperation with one of the most important institution in the Austrian health care system, which was started to optimize the solutions of problems mentioned above and to integrate new modelling approaches for analysis of data. An outline of the different aspects like implementation of big data sets in modelling of diabetes mellitus, comparisons of different modelling approaches, combining such approaches to get more effective models and implementing models based on clinical problems should be given.

Keywords: combined simulation, data models, health care modeling, socioeconomics, complex data

1. INTRODUCTION

1.1. Hybrid Simulation Cooperation

Using combined and hybrid simulation in different areas the working group „Mathematical Modelling and Simulation" at the Vienna University of Technology has gained a wide knowledge about solving problems of combining complex data systems and difficult structures of systems to be modelled. Since 2005 the working group works in cooperation with the HVB (Hauptverband der österreichischen Sozial-versicherungsträger, Abt. Gesundheitsökonomie - Main Association of Austrian Social Security Institutions, Dept. Health Economy) to implement this knowledge in the area of Health Care Modelling.

1.2. Applications & Structure

A main goal is to help the HVB to supply information and knowledge to implement an information platform. This platform should be able to show differences between the current situation and target values and to allow an analysis of complex situations and the identification of problematic situations in different areas of the health care system. Potential fields of activity for actions in the area of the Social Security Institutions or other areas should be identified, mentioned or at least be described. For these tasks appropriate methods and strategies should be provided. Another main goal is to transfer the results to different areas (process owners and decision makers) inside the Social Security Institutions (Figure 1).

Various methods of discrete and continuous modelling and simulation are used and a huge amount of structured or unstructured data sources have to be analysed. The combination of methods like system dynamics, cellular automatons, agent based modelling, differential equations and other modelling techniques have to be compared and sometimes apply within one subsystem. Various Data models have to be mapped, basing on a very complex system of the HVB and the different social security institutions.

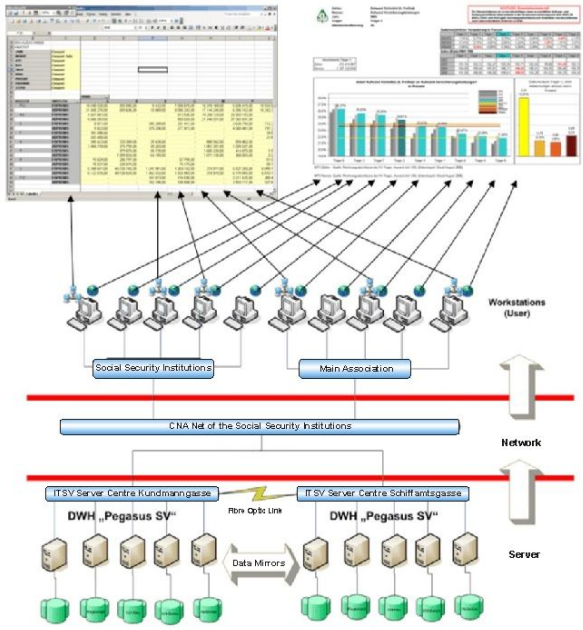

Fig. 1: Structure and Technical Foundation of the Provided Data Sources

A main goal of the project is to improve the state of the art of modelling approaches in health economy to

improve the opportunities in the decision processes. For this reason new data models, new combinations of modelling approaches and an improved possibility of parameter identification have to be provided.

1.3. Subsystems and Model Approaches

As application examples different approaches will be described. First there is the implementation of a System Dynamics model for the incidence of type-2 diabetes in Austria based on a model developed by A. Jones, J. Homer et al. for the United States of America. In this case a huge amount of given data sets had to be imported and integrated into the model. The comparison of classical differential equation methods and cellular automatons for analysis of epidemic models led to results for advantages and disadvantages of the different models. These and other results influenced a combined approach (Cellular Automatons and Agent Based Simulation) for modelling and simulating inhomogenous communities to analyse epidemic influenza scenarios. Finally the implementation of e-information systems to provide information for physicians to cope with PSA measuring.

2. MODELS & IMPLEMENTATIONS

2.1. Using System Dynamics in modelling Diabetes mellitus

Diabetes mellitus (DM) and its complications are one of the most challenging topics in public health care. We adopted a System Dynamic (SD) model, commissioned by the Center for Disease Control and Prevention (CDC) in the USA, which has been successfully applied to reproduce the historical available data of the last two decades. The structure of the model arises not only from the progression of DM as a chronic disease but also from the available data. We adopt the model to the Austrian data set and enhance it to include a distinction by sex since different policies may become necessary.

2.1.1. Decision of Modelling Technique

There were different aspects for the choice of the modeling technique:

1.) Different players in health economy recognize the threat and agree that measures on an population-wide, system-wide level have to be taken to reduce chronic diseases and their consequences. But most programs use conventional analytical methods by which each aspect of a complicated disease control strategy is addressed and evaluated separately. The advantage of SD here is that one gets a global picture where all influencing factors are incorporated and act together.

2.) As chronic diseases involve long time scales there are long delays between causes and health consequences making short term analysis methods unsuitable. Three prevention levels, of which each can require dozens of years of treatment, are distinguished: primary prevention to avoid the onset of an affliction, secondary prevention to avoid chronic development and harmful consequences and tertiary prevention to avoid the loss of functions.

3.) For every prevention level many different policies are available. Primary prevention includes behavioral and socioeconomic measures like improving lifestyle, working and living conditions, information, education and many more. Secondary prevention focuses on precaution and early detection. And finally elements of the tertiary prevention are accessibility to the medical treatment, improvement of compliance and empowerment. SD now gives the opportunity to test different approaches and policies simultaneously and observe the respective outcome.

2.1.2. Modelling Approach

In Figure 2 the population stocks and flows in the model are shown. Seven different population stocks are arranged in four groups. The first group consists only of one stock: the healthy adults who have a normal blood-glucose level. The other groups each consist of two levels, the diagnoses and the undiagnosed ones. The second group is the population with pre-diabetes. These are people with an increased blood-glucose level but not yet having developed full diabetes, which constitute the third group. In the last group are people who not only have diabetes but are also stricken by consequent diseases.

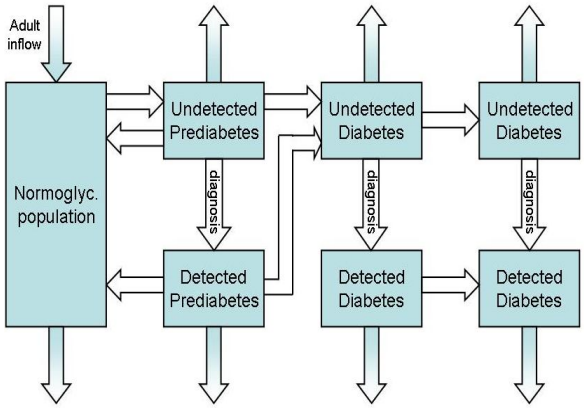

Fig. 2: The main stocks and flows of the model

There is only one inflow of healthy adults into the first level, while people may die out of every level. This inflow is given as a time series input by statistical predictions. The different death rates are affected by the fraction of obese people of every stock, which is calculated in our model, as well as by the fraction of elderly people, which is again given as a time series. The basic assumption is that the relative rates of people with a risk factor compared to people without it remains constant in the respective group. Written explicitly

$$\frac{\mathbf{P}(\text{death} \mid \text{elderly})}{\mathbf{P}(\text{death} \mid \neg\text{elderly})} = const.$$
$$\frac{\mathbf{P}(\text{death} \mid \text{obese})}{\mathbf{P}(\text{death} \mid \neg\text{obese})} = const. \quad (1)$$

holds true for every group, where **P**(a|b) denotes the conditional probability of factor a under condition b. If DM is already detected than also the control of the disease, the "disease management", is influencing the death rates. With suitable initial values the dynamic death rates can then be calculated.

The flows between the different stocks are characterized by the following assumptions: While people with pre-diabetes can still recover, there is no way to cure DM after its onset. DM is a chronic disease after all and once complications occur the damage is dealt and cannot be undone. The onset of pre-diabetes and DM occur unobserved, while complications can also arise even if under medical supervision. All transition rates are affected by the elderly and the obese fractions of the respective populations. The progression rates (the horizontal untitled ones) of the detected populations can be influenced by the clinical management, like prevention measures and compliance. The detection rates (the vertical ones) are more difficult to describe: they are first order exponentially delayed functions of the progression rates as well as the testing frequency and the sensitivity of the tests. Time dependent input data enter in several places of DM detection and control incorporating different possible health policies.

2.1.3. Data Integration

In the original model there are over 134 different input parameters and not all of them can be measured directly. It is therefore necessary to estimate some of the unmeasured input parameters so that the output reproduces available historical data. This is the reason why we start the simulation in 1980 and continue it till 2050.

One major difficulty encountered when modeling diseases in general is the estimated number of unreported cases. Our findings are in fairly good agreement to the WHO estimates of a current DM prevalence of 5 to 7 percent. The exact number of cases is not to be taken intimately, but this isn't our goal anyway. In the application we want to compare different policies of health care management against each other.

For the analysis of the model we use data for Austria, since the quality of the data is very good and many input parameters are available, especially with respect to the distinction by sex. This distinction is made by running the model twice with different input parameters and then adding up the respective results.

The most important influencing factors are: age, clinical management and obesity. The age enters through the fraction of elderly people. The adult population, that is age 20 and above is given by a time series. The fraction of elderly people is calculated as the fraction of people age 65 and above compared to the total populatio. The calculation of the values for each year is done by a spline interpolation of order 3 of the available data. The results change less than one percent if linear interpolation is used.

2.1.4. Testing of Policies

A main part of the model was to develop a system for testing different policies in a kind of qualitative way. As an example for such a possible policy testing we calculated the results of the same test run with the difference that people spend an additional 200 kcal per day.

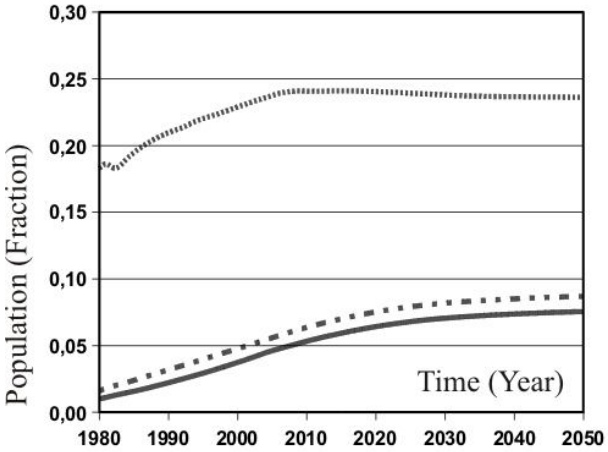

Fig. 3: Pre-diabetes (dotted), diabetes (slash-dotted) and detected diabetes (solid) fractions of the adult population in Austria

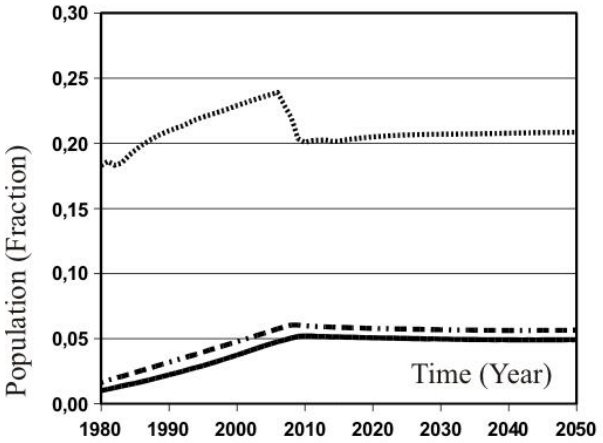

Fig. 4: Same as above - spending additional 200 kcal per day after '05

In Figure 4 we see the same data as in Figure 3 with the difference that people are going for a walk at moderate speed for approximately an hour per day from 2005 onwards.

We see that the growth of the DM percentage stops almost immediately and the pre-diabetes fraction exhibits a sharp drop. The total numbers however are still increasing and only due to a faster increase in the adult population we get a slow decline in the DM rate. This example is somewhat academically since it may not be incorporated in reality. However it shows very nicely that a step-like change in the entry produces a delayed output. While the fraction of the pre-diabetes population is already falling, the fraction of the people with diabetes continues growing for a few more years.

A main goal of the project was to simulate different regions of health care to analyze the west-east gradient of life expectancy and life style in Austria. Together with the HVB and other public decision makers responsible for health care various policies may be tested. Especially interesting is whether different policies for men and women are useful. Ongoing studies to examine the disease management from prevention and early detection over lifestyle adjustment to compliance are suited to validate the predictions made by the SD model.

2.2. Comparison of Different Approaches for a SIR-Epidemic

2.2.1. Problem

Models for the spread of epidemics are nearly as old as the mathematical theory of differential equations. The classical methods applied for modeling such epidemics used to be ODE -Systems but unfortunately these systems are limited in some respect. They become particularly complicated or insufficient when spatial components of disease propagation should be taken into account. This corresponds to the fact that the basic assumption of the classical Kermack – Mc Kendrick (in 1926) model, where the numbers of involved individuals (S, I, R) are described by the following system of ordinary differential equations (ODE).

$$\begin{aligned} \frac{\partial S(t)}{\partial t} &= -\alpha S(t) I(t) \\ \frac{\partial I(t)}{\partial t} &= \alpha S(t) I(t) - \beta I(t) \\ \frac{\partial R(t)}{\partial t} &= \beta I(t) \end{aligned} \qquad (2)$$

is a homogeneous population. Spatial inhomogeneities become especially relevant when vaccination strategies or partitions of the population are observed. In this approach different types of introducing spatial patterns into these dynamics were compared. The applied techniques cover lattice gas cellular automata (LGCA), stochastic cellular automata (SCA) and partial differential equations (PDE).

2.2.2. Different Modelling Techniques

A first step towards to an extended model with better spatial behavior was to define a detailed lattice gas cellular automaton (FHP-LGCA). This approach was validated for the classical structure with the ODE – System. Furthermore vacation strategies where tested and we see that we get better behavior for the whole system.

By stochastic cellular automata (SCA) we refer to ordinary cellular automata (without considering motion of particles) with a stochastically determined neighbourhood. To define a "sociological" neighbourhood in the SCA model, that provides a gradation for the occurrence of interaction between individuals, a decaying likelihood of interaction between cells depending on the distance between them can be used. This approach delivers a radial-symmetric distribution of the contacts for each cell, what principally can be described by an arbitrary probability distribution or a similar function, which we denote likelihood functions.

It is not difficult to show that this approach extends the classical model by a spatial component. The ODEs are again an upper bound concerning the speed of spread and a lower bound for spatial inhomogeneities. If the SCA establishes contact between each two cells (dissolution of the local character and increase of speed), a probability of infection for every individual is obtained.

Finding a connection to the LGCA approach on the contrary is not straight forward. It is possible to find some rules of thumb concerning the weight factors for the SCA, but these rules deliver rather imprecise results and only apply to specific conditions. The difficulty lies in finding a tool that relates motion of particles in the LGCA with distributed contacts in SCA.

Despite this serious difference, we can always find appropriate parameters for the stochastic CA to fit the behavior of the epidemic in the LGCA model. By introducing cyclic motion in the HPP automaton, we minimize the direct interaction area of each individual and thus can easily find a corresponding radius of interaction and the appropriate number of contacts per time step for the stochastic CA. We see, that even without this modification – if the motion in the FHP automaton is determined by standard FHP-I transition rules for example – we can find parameters, which deliver the same quantitative and qualitative behavior. The same is true for the classical SIR model, which requires an infinite radius of interaction and an infinite number of contacts per time step.

Another completely different approach towards an extended SIR model can be by partial differential equations. A modified heat-conduction equation and a suitable discrete solution method was defined with a second order Taylor - polynomial for model simplification. This two dimensional model also fits the time behaviour of the spread of an epidemic in a better way than the classical Kermack – Mc Kendrick equations. We compare the diffusion of the infections from the PDE model with the spread of epidemics in CA models. The advanced CA model is simpler to adapt and fits the real behaviour of an epidemic in an adequate way.

2.2.3. Results

The key output value was the number of currently infected individuals but also a visualisation of the density of infected individuals on the domain permits conclusions on the model behaviours. The input parameters involved the size of the domain (grid size), the number of performed time steps, the disease stage transition parameters, the number of runs used for generating an averaged result (Monte Carlo method)

and the parameter t of the diffusion distribution that was used in the PDE approach. Results are shown in Fig. 5.

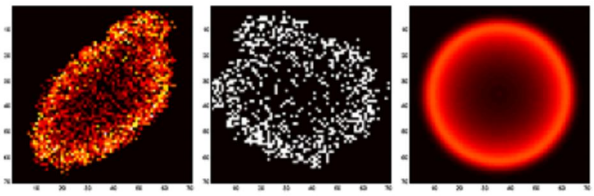

Fig. 5. A lattice representation of the FHP LGCA approach (left), the SCA approach (centre) and the PDE approach (right). Light pixels mark high densities of infected particles and dark pixels mark low densities. This figure does not show specific results but is intended to demonstrate general lattice representations.

An optimal model identification would persist, if the differences are minimal for arbitrary parameter settings. In our case there exist two (heuristic) parameter regions, which deliver good respectively bad correspondence in the model behaviours.

Even though all these methods involve distinct types of spatial interaction, it can be shown, that consistent qualitative and quantitative model behaviour can be obtained by means of parameter adaptions and slight technical modifications. These modifications are motivated by stochastic analysis of distributed interaction (PDE, SCA) and diffusion dynamics (LGCA) as well as prevailing physical analogies. The law of large numbers permits to approximate stochastic contacts by distributed interaction. Diffusion of particles can be approximated through empiric adjustment of a Gaussian diffusion distribution.

2.3. Combined Modelling for Analysis of Influenza Epidemics

2.3.1. Modelling Influenza

In the course of the project to analyse influenza epidemics a hybrid mathematical model was established. The classic methods applied for modelling such epidemics used to be ODE-Systems but unfortunately these systems are limited in some respect. They become particularly complicated and complex beyond limit when observing heterogeneous populations and spatial components. Thus the potential of alternative approaches – namely cellular automata (CA) and agent based systems (AB) – is analysed in the beginning of this work.

Analysis of these methods was split into two major parts. The first one being the theoretical one in which the methods were compared in order to locate their respective strengths and weaknesses. The second part being the practical analysis including behaviour of the implementations.

2.3.2. Combining CA and AB Simulation

In the model an average persons day is divided in three major parts being working time or time at school, leisure time and social life and as a third part time at home respectively sleeping. At the work place, child care facility or school a person is going to meet the same people every day. During leisure time a person usually visits friends, doctors, goes shopping and so on and usually stays within a defined surrounding. The people one meets during this time are often the same. Finally being at home it is assumed that only the family is together. There are no long-distance contacts included. We also do not consider all contacts during the leisure time but simply replace them by a "neighbourhood" of random people.

An Agent based approach to control the whole system and cellular automata to model the subsystems (schools, working places, neighbourhoods, etc.). Such a structure would allow our agents to switch easily from one sub-system to another, without any time gaps within the model. At the beginning of the model the population is randomly initialized with the parameters derived from demographic data. This means that every agent does have a unique ID, a certain health state, an age, a work place (or child care facility respectively school) depending on its age, an assigned household and neighbourhood. Every day all agents move to their work places (respectively schools or child care facilities) and spend the working time there. Excluded from this procedure are senior citizens which are assumed to stay at home during this time. The simulation of the working time is done by cellular automata: every workplace is simulated in a separate automaton. This is convenient to implement and offers great potential for parallelization. This is becoming specially interesting in the near future with increasing numbers of cores on CPUs.

After work the agents proceed to the neighbourhoods which are again simulated separately by cellular automata, thus parallelization is applicable here as well. It would be possible to process several households/neighbourhoods parallel on machines with multiple processors or cores and by this improve the performance of the model. At the end of the day the agents return into their households. Here infection is simulated by simple probabilities since contact between all members of the household can be taken as given. In single households infection is of course not possible

2.3.3. Scenarios

As the advantages are described in chapter 2.2. also the main advantage of this implementation is the possibility to experiment with different policies and even more important in this case with given data sets from the "real life". As an important aspect the model can relative easily be adapted to new findings an results from our cooperation partner. As one quantitative result we found, that the number of infected can be reduced by 45% if every fifth already infected stays at home.

2.4. PSA value changes over time

Additional a project is mentioned that is based on the observation of a quasi – exponential ascent of PSA

(prostate specific antigen) – value during affection on prostate cancer.
The input parameters of the model are three measurements of the marker in the blood of the patient at different times. An important appraisal of the characteristics of the illness is the so called doubling time of the PSA value. Furthermore, after ablation of the prostate, it can be tested with this marker, if parts of the afflicted tissue are still in the body of the patient.
As it is nearly impossible for human beings to find the exact exponential fitting curve through three measurement points and to see when the doubling time of the last measurement occurs, computers are used for calculation. For this reason an internet based tool for assistance in analysis of the behaviour was developed for the users. Important additional features of the new tool, comparing with other systems developed in the USA, are the graphical output of the results for a better comprehension also from the patients and the comparison with a linear approximation curve, which is a common effect for elderly patients. Starting with three measurements a nonlinear optimization with the principle of least square error method is implemented.

One of the main tasks and improvements to other methods is to question the reliability of the results. This second task is dealing with the minimal and maximal doubling time depending on the occurrence of measurement errors.

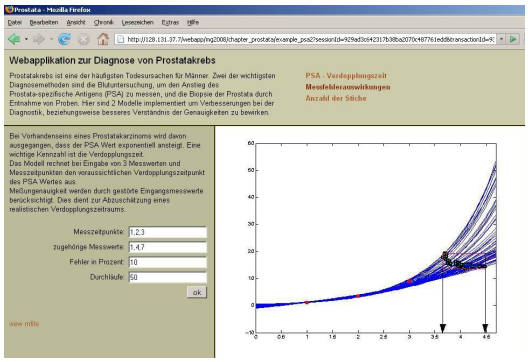

Fig. 6 Solutions with error afflicted input data, the two arrows in the right section of the figure, point out the minimal and maximal doubling time, as calculated for the exponential growth model assumption

The result, which is calculated through solving the solution routine with different randomly disturbed measurement data streams, is visualized by plotting all exponential interpolation curves and an interval, whereby the left boundary is the minimal doubling time and the right sides is the maximum doubling time depending. This is done to help the user defining the next date for new measurements.

2.5. Modelling and Simulation Results

By now the project showed that the possibilities of parameter identification and reaction times for integrating new data sets could be improved. As the diabetes model showed the possibility of working together the models for epidemic problems or technical solutions were the first proves for solving concrete problems and improving the possibilities of modelling and simulation in this field.

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Nikolas Popper has earned a degree in technical mathematics at the Vienna University of Technology. His thesis title is "Simulation of the Respiratory System - Compartment Modelling and Modelling of Perfusion". After research stays abroad in Barcelona, Universitat Politècnica de Catalunya and Moscow, Idaho, University of Idaho, he has experience in industry projects as well as research and development knowledge. Currently he is working in the area of visualization in computer graphics, modeling and simulation of health economy and theory of modeling & simulation. He is co-proprietor of the company “die Drahtwarenhandlung” Simulation Services. The company offers as well technical solutions (defect detection on pictures, modeling & simulation, …) as well as animations and films in the area of Science Journalism. Furthermore he is doing a PhD thesis in the area of alternative and coupled models at the Vienna University of Technology.