HYBRID SIMULATION WITH SIMUL8 - A HEALTH ECONOMICS EXAMPLE

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ABSTRACT

Economic evaluations take place when a new drug or device is being taken to market and is also used by healthcare payers and providers when considering whether to adopt any innovation. Clinicians and administrators need to understand not just whether the new intervention is cost effective when applied to theoretical cohorts of patients, but also what it would mean when implemented in their own organization or health economy. Simulation allows modelers to simulate both the transition between disease states and their likely costs and QALYs as well as to understand how the individual patient will now use services and resources. Using a case study example, this paper demonstrates how health decision-makers can use SIMUL8 simulation software to create a hybrid model for this purpose.

Keywords: Hybrid simulation, SIMUL8, health economic modelling

1 INTRODUCTION

Discrete event simulation is the most widely used simulation technique in industry, but there are also some scenarios where agent or continuous simulation are the right tool for the job. In some use cases, there are also real benefits to combining techniques to create a hybrid simulation. SIMUL8 is a multi-method simulation tool that incorporates, continuous and agent functionality to give users the power to model any scenario. This whitepaper will talk through a use case of health economic modelling to show the benefits of using a hybrid approach and how to achieve this using SIMUL8.

2 THE USE CASE FOR USING HYBRID SIMULATION IN HEALTH ECONOMICS

Research publications are recognizing that economic modelling which does not take into account waiting times and delays and their impact on the effect of treatment and costs can be erroneous. Discrete event simulation combined with agent simulation is being increasingly recommended as an economic evaluation technique.

Clinicians and administrators need to understand not just whether the new intervention is cost effective when applied to theoretical cohorts of patients, but also what it would mean when implemented in their own organization or health economy.

Simulation allows modelers to simulate both the transition between disease states and their likely costs and QALYs as well as to understand how the individual patient will now use services and resources. Decision-makers will need to be assured on all these points prior to approving a business case for implementation of a new way of working or the adoption of a drug or device. Ron Shannon from GHE lists the following reasons to use discrete event simulation, it:

- represents clinical reality
- presents the course of disease naturally with few restrictions
- is flexible: no mutually exclusive branches or states required
- follows the natural concept of time, the simulation clock keeps track of the passage of time (no fixed cycles)
- offers flexibility for handling perspectives and sensitivity analyses

- permits transparency
- allows queuing (e.g., if a health resource is not available at a given time)
- enables modeling of limited resources, bottlenecks, if applicable to the problem
- defines patients as explicit elements with specific attributes (e.g., sex, age, event history) that can be modified over time
- provides the option of updating variables continuously or at specific time periods
- and, in economic evaluations, discrete event simulation has the flexibility to accommodate a richer structure without making it unmanageable in size

While many health economists are using discrete event simulation, others prefer Monte Carlo and Markov models. SIMUL8 simulation software combines state transition modeling with discrete event simulation to allow users to have the full flexibility to model key healthcare questions. This paper will show how to use a hybrid simulation technique to model challenges such as health economics.

3 SIMUL8 CASE STUDY - DISEASE MODEL

The most important part of your simulation will be modeling the disease/condition as the different stages of the disease will determine what treatments, costs or resource are required by the patient. The simplest way to do this in SIMUL8 is to use State Charts.

3.1 State Charts

State Charts allow you describe what is happening to the patient in a supplemental way to a typical discrete process. This significant benefit of using the method is that it removes the need for complicated logic. They describe a series of states (conditions) through which patients will flow. Typically the flow through a series of states is not related to the physical position of the patient. Instead we can link the physical position of the patient by triggering events in a discrete process which depend on which state (condition) the patient is in.

- *States* are used to describe the various condition which the disease can progress through. These could be Low, Moderate or Severe stages of a disease.
- *Decisions* are used when a patient transitions from the state but a decision as to what state they will transition too happens. Such as from the state Low 50% of patients will transition to Moderate and 50% to High.
- *Transition arrows* allow you to control how a patient transitions from one state to another. There are various options to how patient can transition such as chance per day or a distribution of time spent in state.

3.2 Building the Disease Model

To build your disease model simply drag and drop states and/or decision points from the building blocks tab at the left hand side of the . Once all the required states are on screen these can be connected up with transition arrows. To connect states with transition arrows hold down the Shift key and click and drag from state to state to create an arrow. Transition arrows can go both to and from states.

For this guide we will be using an example model to talk through the concepts, the example model is based on a project looking at the cost effectiveness of different treatments for Chronic Venous Leg Ulcers. The disease pathway is outlined in *Figure 1*.

Figure 1 *Leg Ulcer Disease Pathway*

3.3 State Properties

Once you have dropped your required states on screen we can then populate these with properties. State properties are accessed in the same way as any other SIMUL8 object, by selecting the object and using the ribbon menus or by double clicking on the object.

Under the state preferences tab, the first box is where you can name the state. By doing so SIMUL8 will automatically create a Label also with this name as States require Labels to work. Alternatively you can select a pre-defined Label and SIMUL8 will automatically set the name of this state to the Label.

Also within this tab we can define start up values for the states, in the example model in *Figure 1* this is used to define the patient cohort that will be run through the model. All patients will start in the state Uncomplicated Ulcer, to do this enter a value in the box named 'Initial Content'.

3.4 State Transitions

The next step is to define how patients will transition from state to state, to enter these properties double click on a transition arrow. Select a transition type from the drop down menu, a short description of each transition type is provided below:

- *Chance each per time unit*: Enter the chance each patient has of transitioning per time unit.
- *Percent of all per time unit*: Enter the percentage of patients that will transition per time unit
- *Elapsed time in state*: Enter the time it will take for a patient to transition.
- *Rate (number per time unit)*: Enter the number of patients that will transition per time unit.
- *Time of day*
- *One every N time units*: Enter the time at which one patient will transition.
- *All every N time units*: Enter a time unit in which all patients will transition.
- *Always*: Patients entering this state will always transition.

When selecting a transition type it is important to remember that the transitions are based on the simulation time units. By default SIMUL8 sets the simulation time units to minutes. To change these settings go to the Data and Rules tab and select clock properties and select from the required unit from the top. For the ulcer example model select the setting 'Days'. In the ulcer example model there are three transition types used, the first is Chance each per time unit. The table below outlines the values and states that use these transitions.

Table 1 Values and states using transitions

From State	To State	Chance Per Day
Uncomplicated	Death	0.000131
Uncomplicated	Clinical Infection	0.000548
Uncomplicated	Skin Disorder	0.0000224
Clinical Infection	Severe Infection	0.0000167
Severe Infection	Death	0.000141

The transitions Clinical Infection and Skin Disorder back to Uncomplicated and Severe Infection to Very Ill are based on a distribution, meaning that patients are likely to spend a certain amount of time in that state before transitioning. To create distributions select the data and rules tab and distributions, use the data in *Table 2* to create the distributions required for the ulcer example.

Table 2 Defining distributions

Distribution Name	Time in State (Days)	Distribution Type
Clinical Infection	9	Average
Severe Infection	9	Average
Skin Disorder	8	Average

Once the distributions have been created, apply them to correct transition arrow. To do this, first select the transition type Elapsed time in state, use the (...) to open the formula editor and select the correct distribution. Distributions can be found by selection the 'Object' option at the left hand side. *Table 3* shows which distributions should be applied to each transition.

Table 3 Distributions to apply to each transition

From State	To State	Chance Per Day
Clinical Infection	Uncomplicated	Clinical Infection (9,Average)
Skin Disorder	Uncomplicated	Skin Disorder (8, Average)
Severe Infection	Very Ill	Severe Infection (9, Average)

The final transition is that from Uncomplicated to Healed Wound. This is based on a percentage chance of healing which changes each week the patient is receiving treatment. To set up this transition the heal time data needs to be entered into an internal spreadsheet. To do this select the Data and Rules tab, then the information store and create a new spreadsheet. Next, copy and paste the heal time data into the spreadsheet. The heal time data can be found in *Appendix A* of this paper.

The next step is to set the Healed Wound transition, double click the arrow and select the transition type percent of all per time unit. Like with distributions, use the (...) button to reference the spreadsheet. All spreadsheets are found in 'Information'. After selecting the spreadsheet the column and row from which to read the data needs to be specified. The column will always be 2 and the row will be based on the week. There is a MATH function WEEK to control this which will automatically increment the row depending on what week the simulation is running by using the reserved SIMUL8 variable 'Simulation Time'. The images below outline how this should be populated.

Figure 2 How to populate the Formula Editor

The disease model is now complete. Run the simulation for 1 year and you will see patients transition from one state to another. At the end of the run we are able to see the current state of patients and how this has changed from the initial cohort starting in an uncomplicated state.

Figure 3 Completed disease model results

3.5 Sub States

Sometimes you may wish to have sub states within your disease model. By drawing a state wholly within another state, this means that a patient will be represented both in the main state and the sub state. In the ulcer example we have both a clinical infected state and a severe infected state but we may wish to capture information of all infected patients. By drawing a state around both the Clinical infected state and severe state this will allow us to do this. If you run the simulation you will see that patients will appear in both states.

Figure 4 Adding a sub state to the model

3.6 Transition Decisions

These are useful when it is necessary to be able to branch a patients change in transition in a number of different paths. For instance, in the example model we are capturing how many patients are healed over the year but we may also want to capture reoccurrences and feed these back into the disease model. From the data we know that 10% of patients will have a reoccurrence in a year of being healed. Redraw the structure to include what is illustrated.

Firstly, you will need to redo the final transition rule from Uncomplicated to the new transition decision point.

Figure 5 Adding the new transition decision point

By double clicking on the transition decision you can select from 3 routing options. Select percentage and enter 90% to Healed Wound and 10% to Reoccurrence. Lastly define the transition between Reoccurrence and uncomplicated wound, as this can happen at any point in the year select the 'Elapsed Time' option and use a uniform distribution between 1 and 365 days.

3.7 State Actions/Events

State events are a useful feature in being able to produce your own custom results or attaching information to individual patients. State actions/events can be accessed on the ribbon or by double clicking a state. For the ulcer example the total number of Severe Infections, Clinical Infections and Skin Disorders over the year needs to be displayed.

For this global number variables for each result need to be created. These are created in the information store, the same way as the spreadsheet was created. Once these have been created, select the State Action 'On Join' and chose the option 'Change Anything'. Now select the appropriate variable using the formula editor, global variables can be found in 'Information'. Next, choose the Action 'Increment' from the right hand side, this will then automatically increment the variable by 1 each time a patient enters the particular state.

You can also utilize SIMUL8's visual data feature so that you can see these results onscreen. To do so, go to the insert tab and select visual data. Next, click the area on the screen where you wish the data to be displayed and then select from the drop down the appropriate variable. Now run the simulation and you will be able to see on screen the total amount of patients who have entered that state.

Figure 6 Onscreen simulation results

The same principal can be applied if you want to attach information to individual patients. For instance, if you were wanting to record utility values in order to calculate QALY's. In SIMUL8, Labels are used to do this. To create a Label, go to Data and Rules Tab and select Labels. Once you have created a Label, select a state and then as with the global variables you can select either 'Actions on Join' or 'Actions on Leave'. The value of the Label can then be changed to store particular information about that patient. In the ulcer example we can set the utility value for each patient depending on what state they are. In the image below we are setting the utility Label to 0.4 to represent the value associated with being the state 'Severe Infection'.

Figure 7 Changing Label value

In calculating QALY's, the amount of time spent in that state also needs to be recorded. Using another Label called 'Time In', the time at which a patient enters this state can be recorded using 'Action on Join'. Then on using 'Actions on Leave' we can calculate the QALY for that individual patient. First create a Label named 'QALY'. Select the 'Set to' option and chose fixed. You can then use the (...) button to open the formula editor. This allows you to enter a calculation, the below image shows the calculation used in this example. It takes the current simulation time and subtracts the Label value that contains the time that the patient entered the state. This is then multiplied by the utility value and this information is then stored in the Label 'QALY'.

Figure 8 QALY calculation

3.8 Combining the Disease Model with a Discrete Process

State Charts are useful for modelling the disease pathway and how patients transition from different states but it is also useful to be able to combine these with traditional discrete process. For instance, in the ulcer example we want to simulate that the patient will have a hospital stay should they transition into Clinical Infection. To do this, first create the process outlined in *Figure 9* using the traditional SIMUL8 building blocks.

Figure 9 Discrete process simulation model

The next step is to trigger a patient arrival to this process. This can be done by selecting the Clinical Infection state and choosing the Events tabs. Here you can select from all start points in your model and this will cause the patient in the state to arrive at the discrete process.

Before running the simulation make sure that the check box ‘Remove from all states’ is unchecked. This is found by double clicking the End object in the process. If this is checked then when patients have gone through the treatment then they will also be removed from the State Charts. This is a useful feature if an outcome of the process would result in the patient being removed from the disease model. In this example, after treatment the patient will continue to transition in the disease model.

If you run the simulation as is you will get the results shown below, you will notice that the number of arrivals does not match the total number of clinical infections recorded in our results. This is because currently we only have the capacity to treat 1 patient at a time in our discrete process. As you can see from the queue we have a large build up of patients waiting for a bed. Patients are waiting so long for a bed that they have transitioned out of the clinical infection state. At some point over the year they have transitioned back to an infected state but this time an arrival will not be triggered as in reality they are still waiting on a bed.

Figure 10 Combining the disease model with the discrete simulation

This is one of the key benefits of using simulation as you can now start to explore the effect of capacity on your outcomes. By selecting the Activity ‘Treatment for Severe Infection’ we can increase the capacity by using the replicate function found on the activity’s ‘Additional’ tab.

If you increase this to 10 and run the simulation, this problem no longer occurs as we have sufficient capacity to deal with all infections. However, in reality it may be that we don’t have the capacity to. To do this, reduce the replications to 5 and add the additional objects shown below to the process. Next, set the Shelf life of the queue to 3 and the routing in of ‘Treatment for Severe Infection’ to Expired Only. Set the Treatment for severe Infection to a dummy activity by making the activity timing a fixed 0 and ensure the end point has the remove from all states unchecked.

Figure 11 *The expanded discrete event simulation*

The aim of this process is to simulate what happens to patients if they cannot get a bed for treatment of an infection. By setting a shelf life this means that any patient that has to wait longer than 3 days will move down a different path. We now want the simulation to escalate the patients condition, essentially overriding the traditional state transitions, should patients not get a bed within 3 days. As states are controlled via Label values we can do this by using Label actions on ‘Treatment for Severe Infection’. Set the Label Clinical Infection to 0 and the Label Severe Infection to 1.

Now, run the simulation again and we can see that as a result of lack of capacity we have an increased amount of Severe Infections. By modelling this it allows you to think about the effects of capacity on patient outcomes and how this may differ with treatment options.

As well as being able to trigger arrivals and control the State Charts, the time spent in activities can also be linked to the disease model. In the ulcer example patients will require a bed whenever they have a clinical or severe infection. The disease model controls when they will transition back to an uncomplicated state so in the discrete process we want to ensure that the patient will remain in a bed until they transition back to a healthy state.

Select the object Treatment for Infection and on the Ribbon select Additional, then Timing. Choose the bottom option and select Uncomplicated Wound from the list. This will now ensure that the patient will stay in the activity until they transition back to an uncomplicated state.

3.9 Costs

If you have connected your disease model to a discrete process you can use the traditional building blocks to apply costs to your simulation. On each tradition simulation object there is a costs option which is accessed by selecting the object, Properties and Finance. In the ulcer example we can apply a cost per day that would be incurred due to the patient being in a hospital bed.

Cost results are displayed in the income statement which is found on the home tab. This will give you a breakdown of where all the costs incurred in the model are. Like all results in SIMUL8 you can add these to the results summary by hovering over the result and right clicking. This is helpful when comparing runs.

Costs can also be applied using the method discussed in State Actions, where you can increment variables or spreadsheets when a patient enters or exits a state. If you require more complicated cost functions which require rules then you can also access Visual Logic. Each state has a number of events where you can code conditional statements in the Visual Logic editor. Select a state and on the properties tab on the ribbon chose Events, after selecting an event this will then open the Visual Logic editor.

4 CONCLUSION

Disease modeling is just one example where combining discrete event and agent simulation techniques adds value. This combination can also be applied in manufacturing, supply chain, service delivery, or anywhere where you have equipment or resources that degrades over time. With SIMUL8, you can rapidly build simulations that incorporate either individual techniques, or a combination of techniques to model and improve any type of business processes.

A APPENDICES

Table A-1 *Heal Time Data*

From State	To State
Week 1	0
Week 2	0
Week 3	0
Week 4	0
Week 5	0.04
Week 6	0.06
Week 7	0.12
Week 8	0.16
Week 9	0.23
Week 10	0.25
Week 11	0.29
Week 12	0.29
Week 13	0.41
Week 14	0.41
Week 15	0.41
Week 16	0.41
Week 17	0.43
Week 18	0.43
Week 19	0.55
Week 20	0.55
Week 21	0.62
Week 22	0.64
Week 23	0.69
Week 24	0.69
Week 25	0.72
Week 26	0.72
Week 27	0.72
Week 28	0.72
Week 29	0.73
Week 30	0.73
Week 31	0.74
Week 32	0.75
Week 33	0.75
Week 34	0.76
Week 35	0.76
Week 36	0.76
Week 37	0.76
Week 38	0.76
Week 39	0.77
Week 40	0.77
Week 41	0.77
Week 42	0.78
Week 43	0.79
Week 44	0.8
Week 45	0.81
Week 46	0.82
Week 47	0.83
Week 48	0.84
Week 49	0.84
Week 50	0.84
Week 51	0.84