

CHOOSING APPROPRIATE TIME CYCLE LENGTH FOR MARKOV MODELS

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Outline:

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1. OBJECTIVE

The objective of this paper is to present some theoretical and pragmatic foundations for deciding on appropriate choice of the cycle length for Markov models. An analogous problem from the domain of digital signal processing will be presented. As audio technology was making a transition from analog media (vinyl records, analog tapes) to digital (Audio CD, mp3) the technical challenges included an appropriate choice of sampling rates used in conversion from analog to digital signals. This paper presents a conjecture that the signal sampling theoretical framework established by Claude Shannon is informative for the choice of the cycle length of Markov models.

Comparison between Markov models and other models will provide additional tools for a modeler to choose the appropriate cycle lengths for their models. Finally, a variable cycle length Markov model will be used to facilitate empirical search for appropriate length of the cycle, allowing for tradeoffs between run time and expected error. Models with tunnel states will not be considered in this paper.

2. ANALOGY WITH SIGNAL SAMPLING – CHROSNY CONJECTURE

Chrosny's conjecture is that there is similarity between Markov model time cycle and sampling interval in the signal sampling theorem by Nyquist-Shannon ^{1 2}. This theorem has been used in Telecommunications and Digital music standards for decades. It can be stated simply that if we want to reproduce sound with good quality, we need to sample it at least twice as often (fast) as the highest (fastest) frequency we want to reproduce with sufficient fidelity. Since good human hearing range reaches to about 20,000Hz (typically much less than 22,000Hz), the original music CD sampling standard was established at 44,000Hz.

To illustrate the reason for choosing the sampling rate it may be helpful to see the following diagrams:

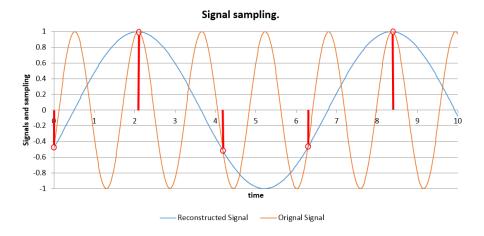


Figure 1

Sampling at ¼ of the original frequency (sampling period is 4 time longer than original signal's period).

In Figure 1 the sampling is done at slower frequency than the original signal. The red bars represent the time points where the sample of the original signal is captured indicated by the red circles. The sample is converted to a digital form representing the magnitude and sign, pictured by the length of the red bar. Such digitized signal can then be used to reconstruct using digital to analog conversion process (as shown by the blue line). The details of filtering the reconstructed signals to arrive at something resembling a sine wave are beyond the scope of this description. If the sampling is done at exactly the same frequency of the original signal the recovery of the signal will not be reliable. If the sampling happens to capture the peaks and valleys as in Figure 2 the signal will be recovered.

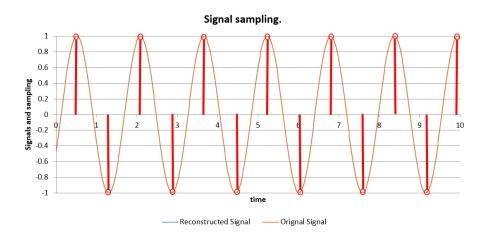


Figure 2

Sampling at same frequency as the original signal frequency (sampling period is the same as the signal's period).

If we are unlucky and the sampling happens at the zero crossing points no signal is recovered as in figure below:

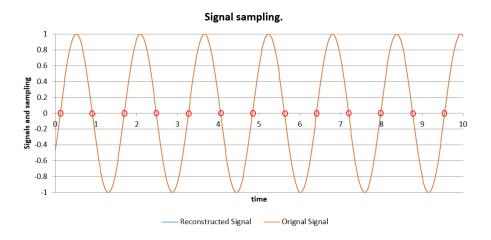


Figure 3

Sampling at same frequency as the original signal frequency (sampling period is the same as the signal's period).

With sampling at twice the frequency of the original signal (higher sampling rate is better), we are guaranteed to avoid recovering incorrect signal (so called 'aliasing problem').

An analogous situation may exist in choosing cycle length (which is equivalent to sampling rate), suggesting that we should consider using cycle length of less than half the shortest length of a phenomena we are trying to model (e.g., 12 hours or shorter for a model that deals with daily hospital stays). In models dealing with less frequent events, the modeler should select the cycle length that minimizes the probability of more than one event happening within a single model cycle.

Chrosny Conjecture

Choose Markov model cycle length that is shorter than half the occurrence interval of the fastest phenomenon you try to model.

The practical limitations on the cycle length depend on actual model run time - similar to practical limitations in signal processing that required higher cost of hardware and software to increase the processing speed. The remainder of this paper will address some practical approaches to establish sufficiently short cycle times experimentally.

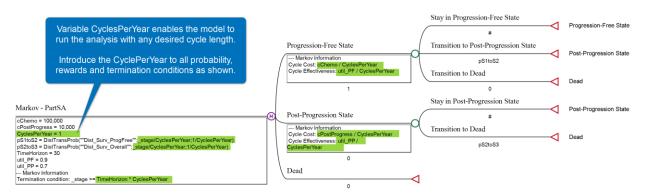
3. Markov models with cycle length as a variable

Most often Markov models are built with a fixed cycle length, chosen *a priori* by the modeler. They are the simplest types of Markov Models for both cohort and individual patient simulations. However, building a version of such models where cycle length is a variable is only moderately more complicated.

The ability to run sensitivity analysis on the cycle length is a great way to experimentally establish what cycle length is sufficiently short and trade it off against expected run time.

An interesting case study of continuous time Partitioned Survival model conversion to variable cycle length Markov model is discussed in the white paper "Equivalence of Partitioned Survival and Markov models" ³ TreeAge Pro can automatically convert a PartSA model to a Markov model that is instrumented with a variable cycle length.

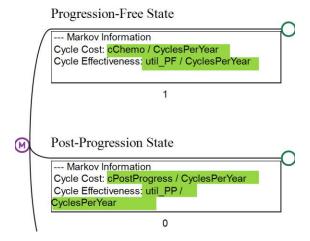
The converted Markov model includes a new parameter CyclesPerYear. This parameter is used to change the Markov model's cycle length. Increasing CyclesPerYear shortens the cycle length and improves the accuracy of the results with respect to the original PartSA model. The CyclesPerYear value affects transition probability calculations in the complex expressions. Annual Costs and Utilities from the PartSA model are divided by CyclesPerYear to generate appropriate values for the cycle length. Also, the termination condition uses TimeHorizon multiplied by CyclesPerYear to make sure that consistent TimeHorizon is maintained for different cycle lengths.



Below are the "zoomed in" sections of the model with the relevant CyclesPerYear expressions.

Markov - PartSA

```
cChemo = 100,000
cPostProgress = 10,000
CyclesPerYear = 1
pS1toS2 = DistTransProb(""Dist_Surv_ProgFree"";_stage/CyclesPerYear;1/CyclesPerYear)
pS2toS3 = DistTransProb(""Dist_Surv_Overall"";_stage/CyclesPerYear;1/CyclesPerYear)
TimeHorizon = 30
util_PF = 0.9
util_PP = 0.7
--- Markov Information
Termination condition: _stage >= TimeHorizon * CyclesPerYear
```

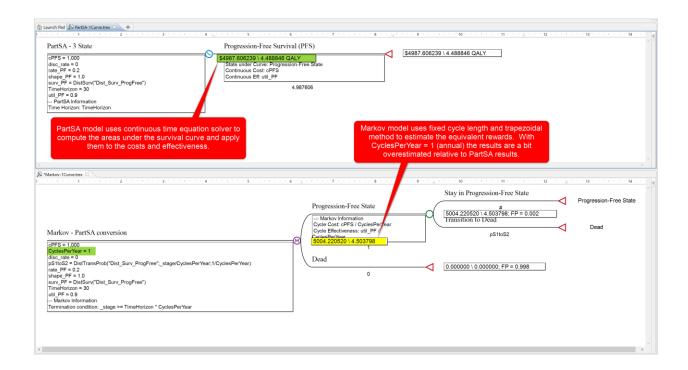


As can be seen the introduction and utilization of the cycles per year variable is not overly complicated and can easily be done as the model is being built. While it is possible to introduce adjustable cycle length to an existing model, the complexity of that task depends on the complexity of the model itself. There are many search and replace features within TreeAge Pro that are helpful in this process, but it is a bit more complex than building adjustable cycle length in from the start.

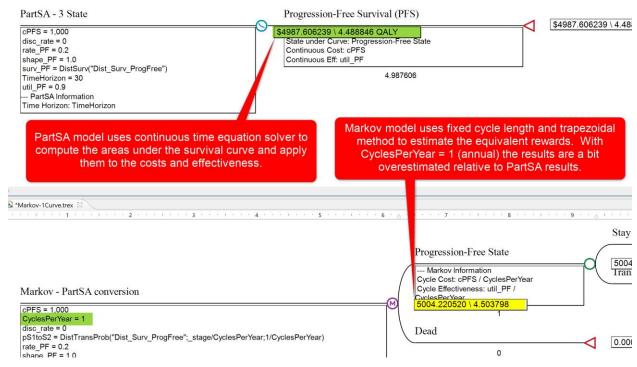
It should be noted that cycle length is varied between simulation runs and remains constant during any a specific simulation. While it is possible to create models which change the cycle length during a single simulation, these models are beyond the scope of this paper.

4. Using other models as references (DES, Partitioned Survival Analysis).

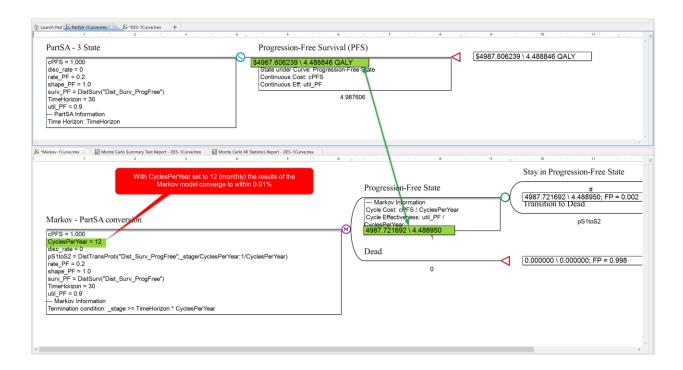
There are a number of different simple examples models showing equivalence of results between PartSA (PartSA-1Curve.trex) and Markov model (Markov-1Curve.trex). An equivalent DES model is also included (DES-1Curve.trex) and can be used as a reference for comparison with other models.



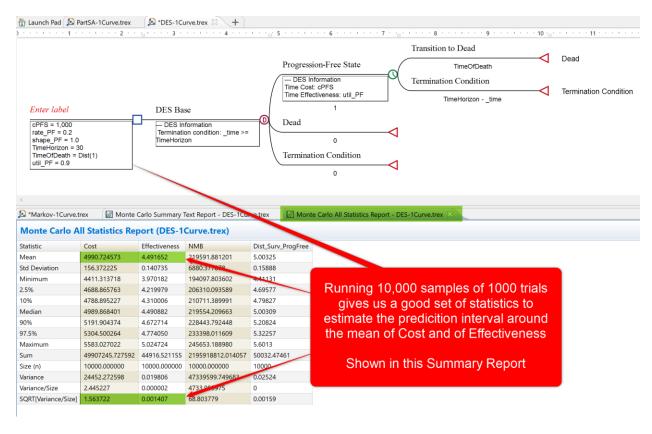
Zooming in on the relevant results:



If we change the CyclesPerYear to 12 (monthly cycle), the Markov results will approximate the PartSA results to within less than 0.01%:



An equivalent DES model can be used as a reference as well. However, DES models have to use a Monte Carlo simulation and not a simple rollback expected value calculation. The example below shows the results of a simulation of 10,000 samples of 1,000 trials each. The summary report can be used for estimating the prediction interval of the mean costs and effectiveness.



Exporting the summary report to Excel and adding some basic formulas for 95% prediction interval of the means gives the following results:

Statistic	Cost	Effectiveness
Mean	4988.149169	4.489334252
Std Deviation	156.7140807	0.141042673
Minimum	4428.283784	3.985455406
2.5%	4680.930057	4.212837052
10%	4788.126527	4.309313874
Median	4986.104767	4.48749429
90%	5186.350679	4.667715611
97.5%	5305.225846	4.774703262
Maximum	5662.223644	5.09600128
Sum	49881491.69	44893.34252
Size (n)	10000	10000
Variance	24559.30308	0.019893035
Variance/Size	2.455930308	1.9893E-06
SQRT[Variance/Size]	1.567140807	0.001410427
Desired Prediction confidence %	95%	
Inverse Normal statistic at the desired level	1.959963985	
Upper bound of the mean Prediction Interval	4991.220708	4.492098638
The Mean estimate	4988.149169	4.489334252
Lower bound of the mean Prediction Interval	4985.077629	4.486569866

The DES results agree well with the PartSA results and monthly cycle Markov results.

Note that such close convergence depends on the shape of the survival curve. If the rate and shape of the distribution is changed using the parameters (rate_PF and shape_PF), convergence will change depending on how fast the survival curve decays. (For example, setting the rate to 5 and shape to 10 and time horizon to 1, and then comparing the results at different CyclesPerYear.)

Obviously the more realistic Markov models can have a much more complicated structure and capture transitions, which cannot be represented within PartSA models. PartSA models rely on assumption that transitions are only made toward sicker states and eventually to the dead state, they cannot be used as a reference for more complicated Markov models. However, DES models can replicate any Markov structure and tend to run more efficiently than Markov models, so they can be used to compare and double check results of Markov models.

5. Empirical assessment of appropriate cycle length.

Another way to assess if the cycle length is sufficiently short is to use the one-way sensitivity analysis on the CyclesPerYear variable and observe how the results converge to a stable set.

For example, using the same Markov example model (Markov-1Curve.trex) and running one-way sensitivity analysis with CyclesPerYear starting at 1 and ending at 141 with 14 intervals will generate the following results:

CyclesPerYear	Cost	Eff
1	5004.22052	4.503798468
11	4987.743638	4.488969274
21	4987.643938	4.488879544
31	4987.623539	4.488861185
41	4987.616129	4.488854516
51	4987.612631	4.488851368
61	4987.610707	4.488849636
71	4987.609537	4.488848583
81	4987.608773	4.488847896
91	4987.608247	4.488847422
101	4987.607869	4.488847082
111	4987.607588	4.48884683
121	4987.607375	4.488846637
131	4987.607208	4.488846487
141	4987.607075	4.488846368

Depending on the desired level of accuracy (how far the cost-effectiveness decision point is from the threshold) and practical run time of the model is, cycle time length can be chosen appropriately.

6. Conclusions.

It has been a common knowledge that shorter cycle times increase the accuracy of Markov model estimates. In this paper we tried to offer some practical ways to confirm this fact and offer ways of instrumenting models to facilitate experimenting with variable cycle lengths. The use of Partitioned Survival Analysis and Discrete Event Simulation models as references to confirm the Markov results was demonstrated. Finally, an analogy to signal processing's choice of sampling frequency established by Claude Shannon was highlighted as a practical rule of thumb: to use cycle length at least half the length of typical events being modelled. We are not aware of any detail mathematical proofs similar to Shannon's theorem in the domain of Markov models, but such research might be of interest in the future.

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