MARKOV MODEL CALIBRATION OF WEIBULL DISTRIBUTED TRANSITION PROBABILITIES USING SCIENTIFIC PYTHON

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OBJECTIVES

Decision-analytic models require a calibration step when model parameter values are not directly observable but can be fitted to external data. Our objectives were to (1) assess the performance of different optimization algorithms to calibrate a simple Markov model with transition probabilities to match observed cohort proportions at three different times, (2) compare the run times and achieved goodness of fit metrics, and (3) inform best strategies for using optimization algorithms to calibrate models.

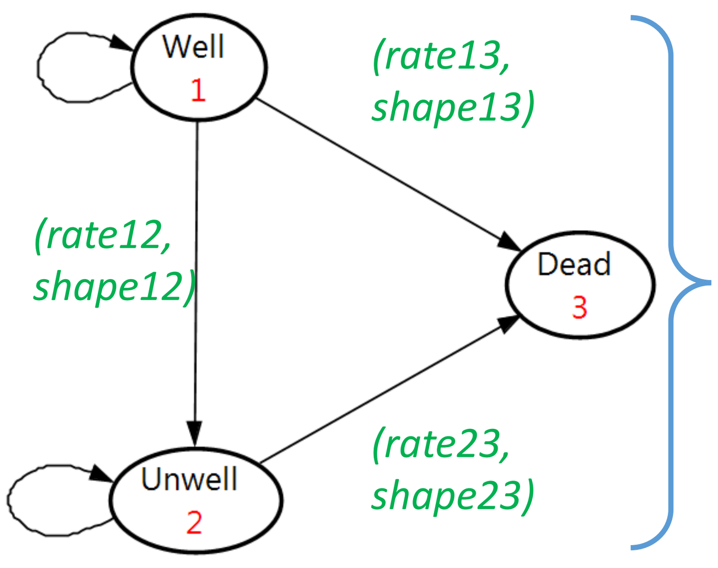
METHODS

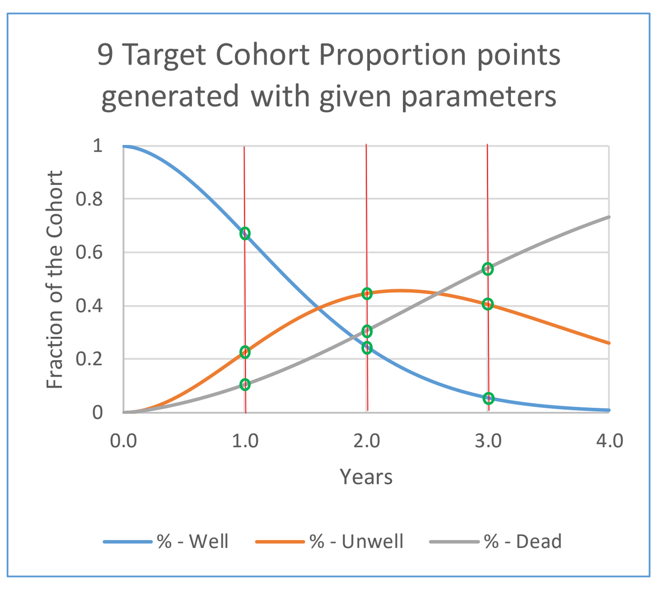
A 3-state (Markov) state-transition cohort model describing simple disease progression served as reference. Transition probabilities are described by Weibull distributions defined by rate and shape parameters. The model is calibrated to observed cohort proportions generated by hypothetical "given" Weibull parameters. Calibration was applied using Scientific Python package with 11 different optimization algorithms (including hill-climbers, stochastic and hybrid types). 50 different initial sets of values of the 6 parameters where used consistently for all 11 algorithms. The sum of squares of differences between simulated calibration target parameters (cohort proportions) and estimated model outcomes proportions is used as goodness of fit (GoF) metric of at least 1E-05.

CALIBRATION TARGETS

Six Weibull distribution function parameters adjusted by optimization algorithms to match 9 data points generated by "given" parameters.

Given Parameters					
rate12	shape12	rate13	shape13	rate23	shape23
0.3	1.9	0.1	1.4	0.2	1.5



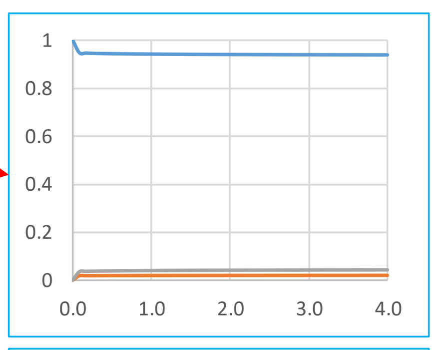


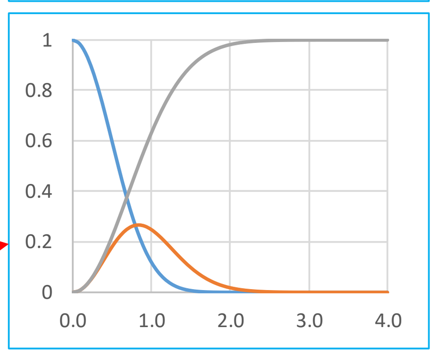
INITIAL PARAMETERS FOR OPTIMIZATION

50 different initial values of rates and shapes used for evaluation of robustness of the optimization algorithms.

Initial Parameters					
rate12	shape12	rate13	shape13	rate23	shape23
0.020	0.030	0.040	0.050	0.060	0.070
0.020	2.000	0.680	0.050	0.060	0.070
1.000	0.030	0.360	2.000	0.060	0.070
0.347	1.343	0.360	2.000	0.060	0.070
0.673	0.030	1.000	0.050	0.373	0.070
⋮	⋮	⋮	⋮	⋮	⋮
0.020	1.343	0.680	1.350	0.687	2.000
0.347	1.343	1.000	2.000	0.687	2.000
0.673	0.687	0.680	0.050	1.000	2.000
0.347	2.000	0.360	0.700	1.000	2.000
0.673	0.687	0.360	1.350	1.000	2.000
1.000	2.000	1.000	2.000	1.000	2.000

Cohort progressions with selected initial parameters

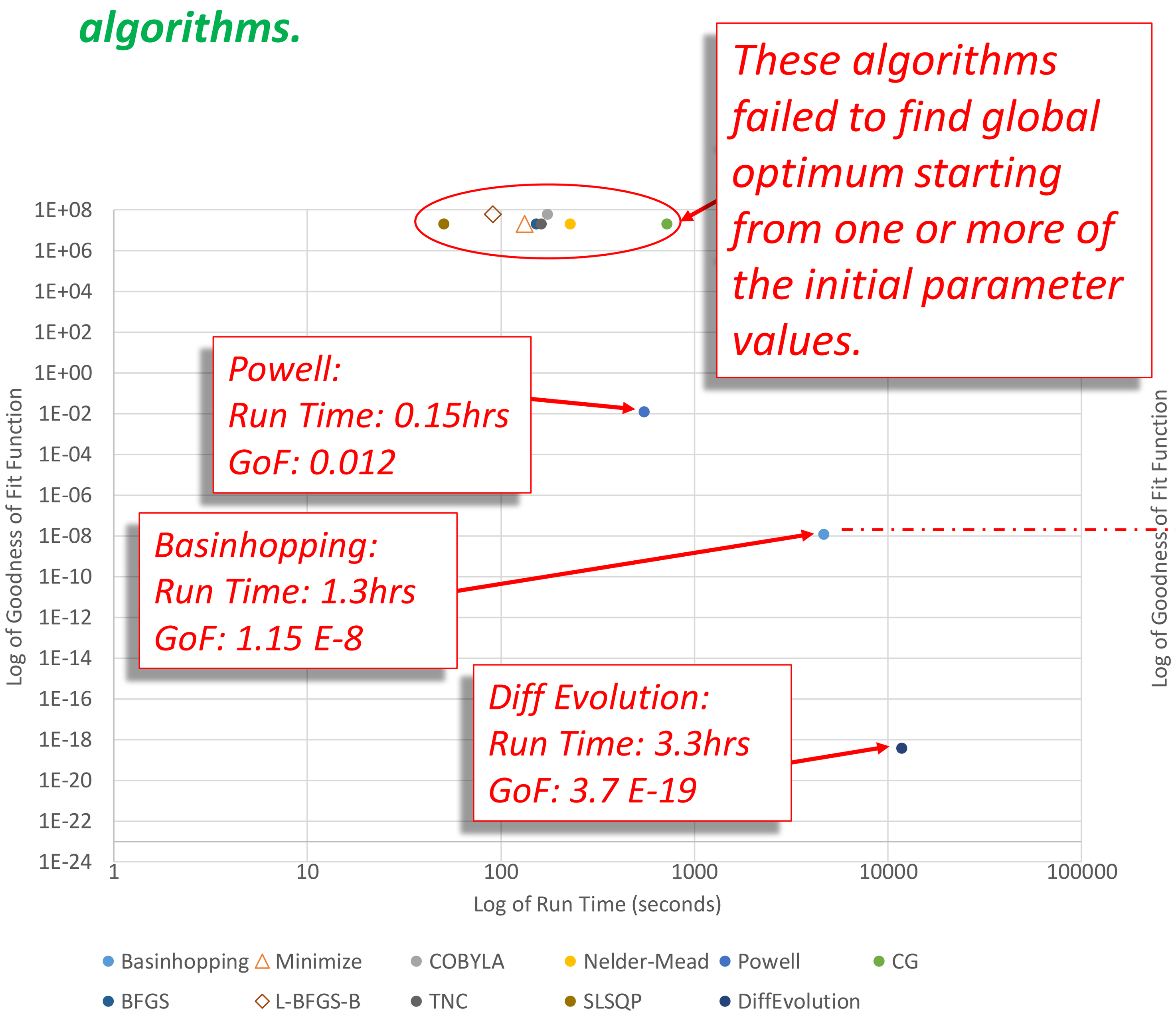




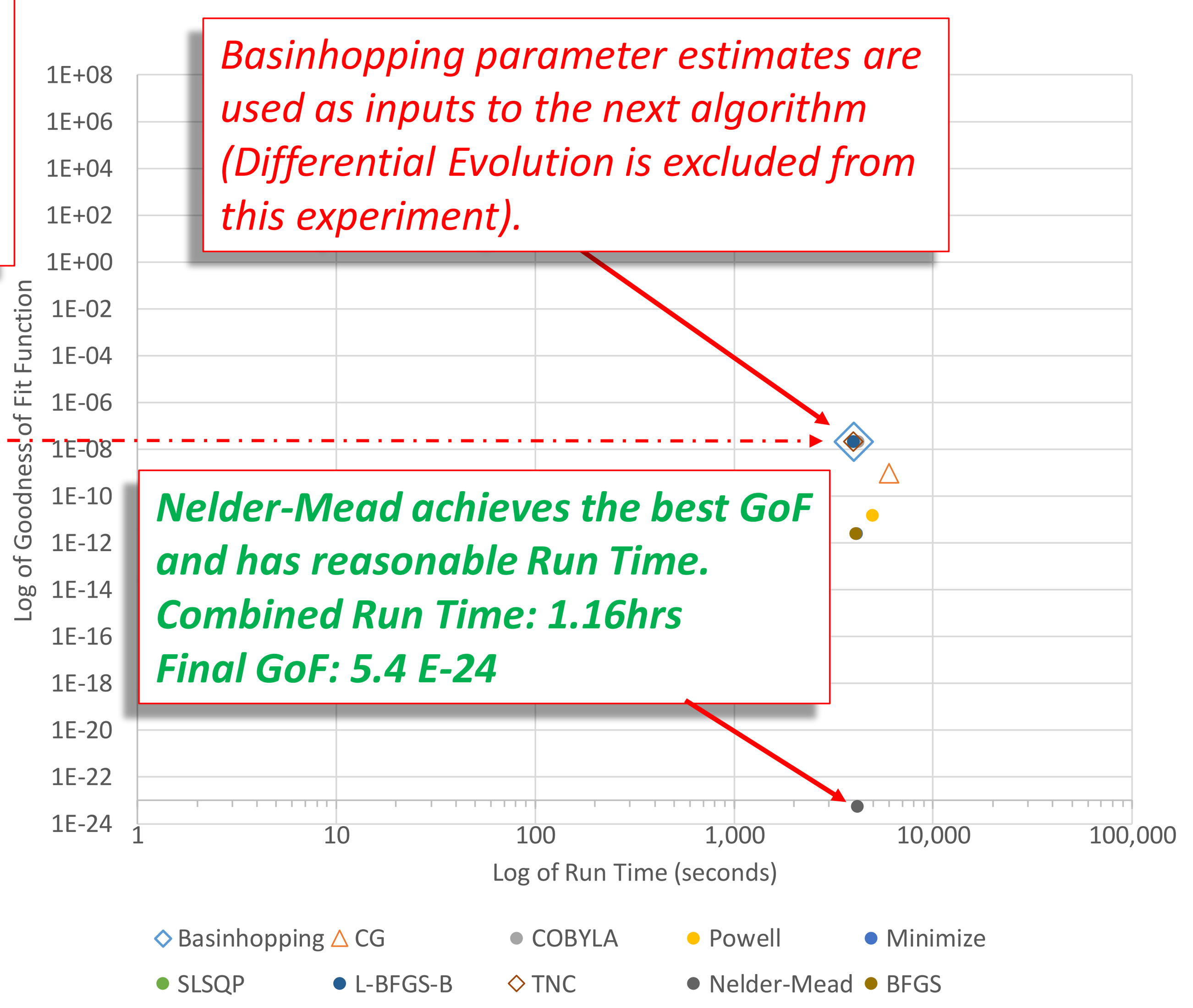
RESULTS

The 11 optimization algorithms found in scientific Python library can be categorized as hill-climbing, stochastic or hybrid types. The hill-climbing types tend to be 2 orders of magnitude faster (several minutes) than stochastic types fast, but are prone to identify local minima far away from actual solution (Goodness of Fit on the order of 1E-03). The stochastic algorithms are more robust in finding global minima, however they require on average 1 hour or more of run time to find a solution in order to reach (Goodness of Fit on the order of 1E-08). The hybrid Nelder-Mead algorithm is able to find good solution provided the initial parameters are "close enough" to the actual values. It is sensitive to the initial values of the parameters and fails to achieve GoF of 1E-05 86% of the time. The only 2 algorithms that consistently found global solutions are the stochastic types (Basinhopping - Average run time of over 1hr and GoF 1E-08 and Differential Evolution – over 3hrs running time and an GoF of 3E-19). Another set of experiments used a pair of algorithms to identify global solution. A stochastic algorithm ran first followed by one of the hybrid or hill-climbing types. The "pair of algorithms" approach resulted in identifying the best pair to be Basinhopping algorithm followed by Nelder-Mead (over 1 hour average run time and average GoF 5E-24).

Calibration with each of 11 optimization algorithms.



Calibration with pairs of optimization algorithms (Basinhopping followed by each of the other 9 algorithms.



CONCLUSIONS

Calibrating 6 Weibull parameters within a Markov Cohort model allows an assessment of performance of different optimization strategies and also to develop hybrid approach of using combination of algorithms. Some algorithms allow the search space to be restricted, which is desirable feature for Weibull parameters which have to be strictly positive. The combination of stochastic and hybrid algorithms used sequentially has been confirmed as the most robust approach which avoids local minima and requires reasonable run time.

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