

Application of the computational method

The experimental data used for parameter estimation consisted of a) the mean duration of the passage experiments j $\bar{\mu}_{\text{exp}}(j)$ and their standard deviation $\bar{\sigma}_{\text{exp}}(j)$ (see Fig. 3) and b) the respective types of mutations and reversions q that occurred (see Fig. 1; these mutational events gave rise to the respective candidate models Θ_i).

In order to use the programmes provided in supplementary material S3, start “EstimateMutationalParameters.m” in MATLAB[®]. The program imports the experimental data (passage times, mutations) and generates candidate models Θ_i for parameter estimation. For each candidate model Θ_i , parameters are estimated 50-times using eq. (11) with random initial values. Estimated parameters and goodness-of-fit (in terms of the residual error $\varepsilon(\Theta_i)$) for each candidate model are written into an output file. The program “EstimationStats.m” can then be used in order to derive statistics for the estimated parameters.