The free energy of a state relates directly to the stationary probability of being in state when the system is in equilibrium, where , where is the left eigenvector of the row-stochastic transition matrix with eigenvalue which relates to the equilibrium state (since .) Since for all , there exists only one eigenvalue of unity and hence is unique.[[1]](#footnote-0)

The stationary probability is related to the Gibbs’ free energy by where is the Boltzmann constant and is temperature in Kelvin.

Then the change in from some reference state is .

**Uncertainty of Free Energy Calculation**

Assume is known. Assume eigenvalues . (This should be tested.)

For an n-dimensional transition matrix , the eigenvector is given by which is a system of n linear equations. .

The computation involved in determining the uncertainty in each value in a n-dimensional system of linear equations is NP-hard.[[2]](#footnote-1) It may be more feasible to run a series of trials where each is given a random value within the bounds of .

Ref 6 gives a sub-optimal algorithm which generates a solution in , in which an ellipsoid in is given in which all possible solutions lie. However, for our applications it is only necessary to attain the uncertainty of the free energy, which relies on uncertainties of individual entries of the vector , and hence a minimum bounding box (hyperrectangle) is sufficient.

It is therefore perhaps possible to manipulate entries of within their uncertainties to intentionally evaluate each entry of at its maximum and minimum. On a toy 2D scale, demonstrations show that taking the minimum and then maximum values for all gives eigenvectors which bound randomly generated eigenvectors >96% of the time.

Unfortunately, on scaling up to 50 dimensional, these upper and lower bounds bound as little as 40% of the data. This method is clearly inadequate on the generated data but is heavily dependent on the magnitude of the fractional uncertainty.

## <http://www.jstor.org/stable/2157442?origin=JSTOR-pdf>

## SIAM Journal on Numerical Analysis

## Derivatives and Perturbations of Eigenvectors

Carl D. Meyer and G. W. Stewart

**Alternative method for calculating free energy**

The partition function of the FE barrier separating states i and j, Zij, is equal to the value of minimum cut between the states in the graph, which can be calculated by the Ford–Fulkerson algorithm (18). After calculating the minimum cuts (FE barriers) between every pair of nodes (clusters), which can be done with only n-1 total minimum cuts for n nodes by use of the Gomory–Hu algorithm (19), the TRDG (4) is constructed to obtain a detailed representation of the FES. Following Becker and Karplus (1) and taking into account that Fij is proportional to kT ln(Zij), one starts with the largest Zij (smallest Fij) and successively connects states in order of decreasing Zij (increasing Fij).

1. Swope W. C., Pitera J. W., and Suits F., J. Phys. Chem. B 108, 6571 (2004).10.1021/jp037421y [[Cross Ref](http://dx.doi.org/10.1021%2Fjp037421y)] [↑](#footnote-ref-0)
2. ## http://www.eecs.berkeley.edu/~elghaoui/Pubs/Ell\_bnds\_uncert\_Aut2004.pdf

   [↑](#footnote-ref-1)