D Monte Carlo method for calculating $r(k)$ from a network with heterogeneous states and distributed rates

To numerically determine $r(k)$ associated with a known network, we use a Monte-Carlo simulation with N trials in order to estimate a mean $r(k)$. The procedure is as follows:

- For each trial, each pool i is fractionated into sub-states j as shown in Figure 2. For these simulations we divide the pools into a total number of n sub-states. The rates k_{ij} and/or the conversion fractions f_{ij} associated with each state are randomly assigned. Each state is assigned an equal partitioning $p_{ij} = 1/n$ because the stochastic information is contained in the random assignment of k_{ij}.
- For each trial, ℓ, the matrix A_ℓ is generated based on the values of k_{ij}, p_{ij}, and f_{ij} for each state and each connection.
- We then calculate the eigenvalues and eigenvectors of $\mathbf{A}_\ell$ and use equation (19) to calculate the eigen-decay state partition $\mathbf{r}_\ell$ for each trial.
- The previous three steps are repeated N times to generate an ensemble of initial eigen-state vectors $\mathbf{r}_\ell$.
- After removing outliers containing degenerate eigenvalues, we divide the $\ln k$ axis into equally spaced bins of width $\Delta \ln k$ and sum the weights r_i in each bin from all trials ℓ. Because the bins are logarithmically-spaced, we estimate the exit rate function in log-rate space $v(\ln k)$. $v(\ln k)$ is related to $r(k)$ by $r(k) = v(\ln k) d \ln k / dk$.
- We then divide the sum by the factor $N \Delta \ln k$ to provide the estimate

$$\mathbf{v} = \frac{\sum_{\ell=1}^{N} \mathbf{r}_\ell}{N \Delta \ln k}. \tag{D.1}$$

$\mathbf{v}$ is a discrete approximation of the continuous function $v(\ln k)$.