| Method                          | Start/End State                      | MFPT       | 5% Confidence | 95% Confidence |
|--------------------------------|--------------------------------------|------------|---------------|----------------|
| CME - numeric benchmark        | Basin centers                        | $1.84 \times 10^5$ | —             | —              |
| Conventional SSA simulation    | Basin centers                        | $1.82 \times 10^5$ | $1.67 \times 10^5$ | $1.98 \times 10^5$ |
| WE - rate mode                 | Basin centers                        | $1.82 \times 10^5$ | $1.78 \times 10^5$ | $1.85 \times 10^5$ |
| WE - transition matrix mode    | Coarse-grained polarized phenotype   | $2.34 \times 10^5$ | —             | —              |
| Coarse-grained phenotype network | Coarse-grained polarized phenotype   | $1.70 \times 10^5$ | —             | —              |

**Table S6.** Computed Mean First Passage Times in the ExMISA Network—Comparison of Different Methods. Computed Mean First Passage Times (MFPTs, time-units $k^{-1}$) of the ExMISA network, using different computation methods. For each row, $\text{MFPT}_{XY} = \text{MFPT}_{YX}$ due to symmetry in the network, and the start- and end-state ($X$ and $Y$) for the transition are defined either with respect to distance from the centers of the polarized phenotype basins, or in terms of aggregated states in the coarse-grained phenotype definition. For basin centers, State $X$ is defined as a hypersphere of radius 1 centered around the state vector $[4,16,0,0,1,0,1,0]$, corresponding to the species: $[a,b,A_{00},A_{10},A_{01},B_{00},B_{10},B_{01}]$. State $Y$ is a hypersphere centered around $[16,4,0,1,0,0,1,0]$. For the coarse-grained phenotype definition, states correspond to the polarized $a/b$ hi/lo and lo/hi phenotypes.