Electronic Supplementary Information (ESI)

Coupling of mitochondrial population evolution to microtubule dynamics in fission yeast cells: A kinetic Monte Carlo study

Electronic Supplementary Information

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1 Flow charts for the different KMC algorithms

1.1 M1 model

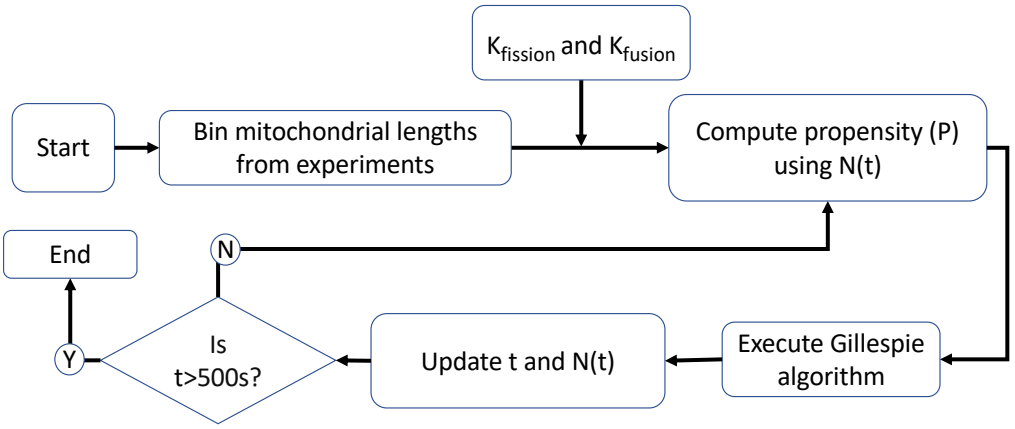

Figure S1 M1 model algorithm: Flowchart represents various processes implemented in the Gillespie algorithm. The fission ($K_{fission}$) and fusion (K_{fusion}) rate constants along with the number of mitochondria (N(t)) are used in computation of propensities.

1.2 MT model

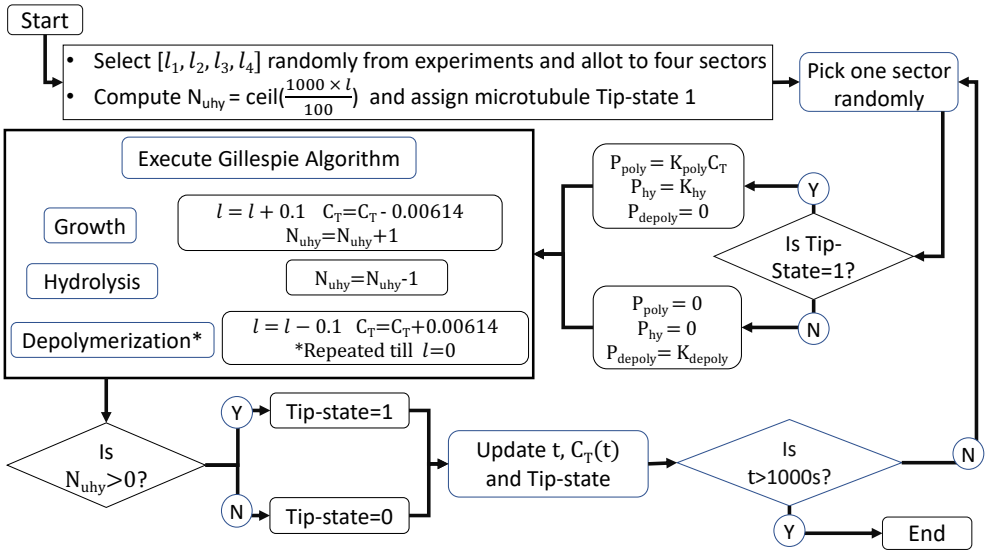

Figure S2 MT model algorithm: In all sectors, the microtubules are evolved from an experimentally observed lengths $[l_1, l_2, l_3, l_4]$ and the number of unhydrolysed units (N_{uhy}) are calculated and the tip-state is initiated with state value 1. Tip-state 1 is assumed for a GTP-bound state of the cross-section and tip-state 0 implies a GDP-bound state of the microtubule bundle. In the model, the GTP bound units are assumed to be adjacent to each other. Using growth (K_{poly}), hydrolysis (K_{hy}) and depolymerization (K_{depoly}) rate constants and the tubulin concentration(C_T), the total propensity (P_T) is calculated and Gillespie algorithm is used to update the time (t) , concentration (C_T) and the tip-state.

1.3 M1MT model

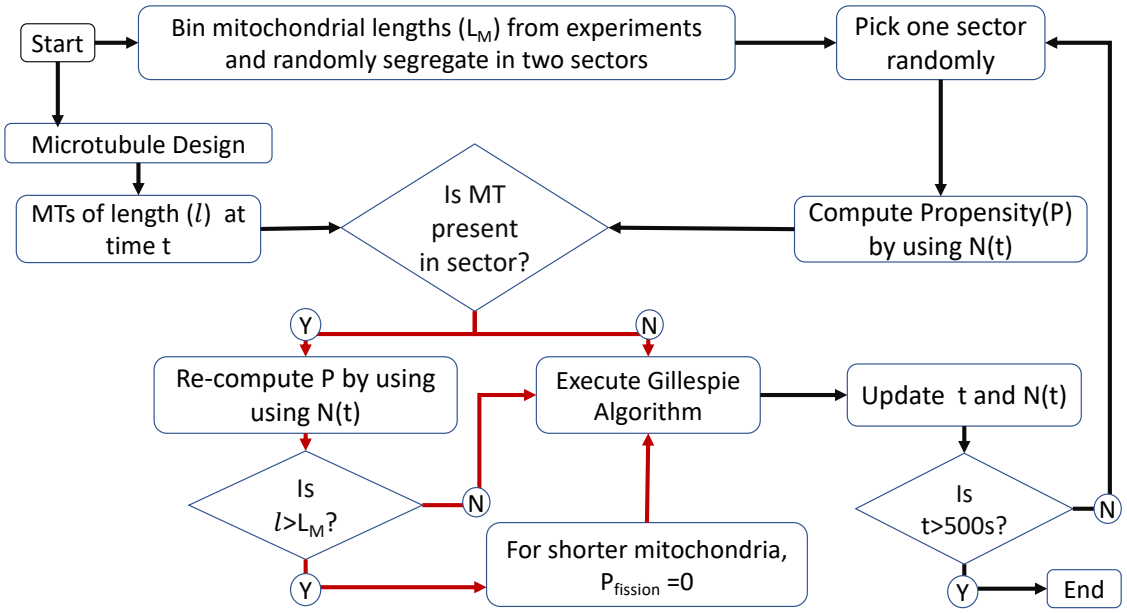

Figure S3 M1MT model algorithm: Mitochondria are binned and in each sector depending on the mitochondrial length (L_M) and microtubule length (l), the propensity of fission ($P_{fission}$) is obtained and state is evolved using the Gillespie algorithm.

2 Description of microtubule parameters

2.1 Elongation velocity

In a particular sector of length $l_s = 5.8$ μm, for growth of 0.1 μm of microtubule bundle at every polymerisation event, let $l_i, i \in (1,58)$ be the length traversed by the microtubule (Fig S4) in the time interval Δt_j^{el} without encountering a catastrophe, then the elongation velocity ($V_j^{l_i}$) at length l_i for the j^{th} instance is defined as ,

$$V_j^{l_i} = \frac{l_i}{\Delta t_j^{el}} \tag{1}$$

The average elongation velocity ($\overline{V}^{l_i}$) at a particular length l_i is defined as,

$$\overline{V}^{l_i} = \frac{1}{M}\sum_{j=1}^{M} V_j^{l_i} \tag{2}$$

where, M is the total number of instances during the entire simulation in which V^{l_i} is calculated at l_i.
The average elongation velocity $\overline{V}_e$ for the microtubule in a particular sector is obtained as follows:

$$\overline{V}_e = \sum_{i=1}^{N} \overline{V}^{l_i} P(l_i) \tag{3}$$

where, P(l_i) is the probability distribution of lengths l_i computed from the the entire simulation, N is the number of lengths (l_i) at which elongation velocity ($\overline{V}^{l_i}$) is calculated. Thus, the overall elongation velocity ($\overline{V}_{ev}$) is obtained by taking the mean values of $\overline{V}_e$ from each of the four sectors.

2.2 Shrinkage velocity

In a particular sector of length $l_s = 5.8$ μm, for shrinkage of 0.1 μm of microtubule bundle at every depolymerization event, let $l_i, i \in (1,58)$ be the length traversed by the microtubule (Fig S4) in the time interval Δt_j^{sh} after encountering a catastrophe, then the shrinkage velocity($V_j^{l_i}$) at length l_i for the j^{th} instance is defined as,

$$V_j^{l_i} = \frac{l_i}{\Delta t_j^{sh}} \tag{4}$$

The shrinkage velocity($\overline{V}^{l_i}$) at a particular length l_i is defined as,

$$\overline{V}^{l_i} = \frac{1}{M} \sum_{j=1}^{M} V_j^{l_i} \tag{5}$$

where, M is the total number of instances during the entire simulation in which V^{l_i} is calculated at l_i.
The average shrinkage velocity $\overline{V}_s$ for the microtubule is obtained using,

$$\overline{V}_s = \sum_{i=1}^{N} \overline{V}^{l_i} P(l_i) \tag{6}$$

where, $P(l_i)$ is the probability distribution of lengths l_i computed from the entire simulation, N is the number of lengths (l_i) at which shrinkage velocity ($\overline{V}^{l_i}$) is calculated. Thus, the overall shrinkage velocity ($\overline{V}_{sv}$) is obtained by taking the mean values of $\overline{V}_s$ from each of the four sectors.

2.3 Catastrophe Frequency

For a particular replicate executed for 1000 s, the catastrophe frequency ${f_c}^r$,

$${f_c}^r = \frac{n_c}{1000} \tag{7}$$

where, ${f_c}^r$ is the catastrophe frequency and n_c is the number of catastrophes observed in that particular replicate.

The catastrophe frequency, f_c^{MT} for a microtubule is obtained by averaging over the total number of replicates;

$$f_c^{MT} = \frac{1}{M} \sum_{r=1}^{M} {f_c}^r \tag{8}$$

where M is the total number of replicates

Thus, the overall catastrophe frequency ($\overline{f}_c$) is obtained by taking the mean values of f_c^{MT} from each of the four sectors.

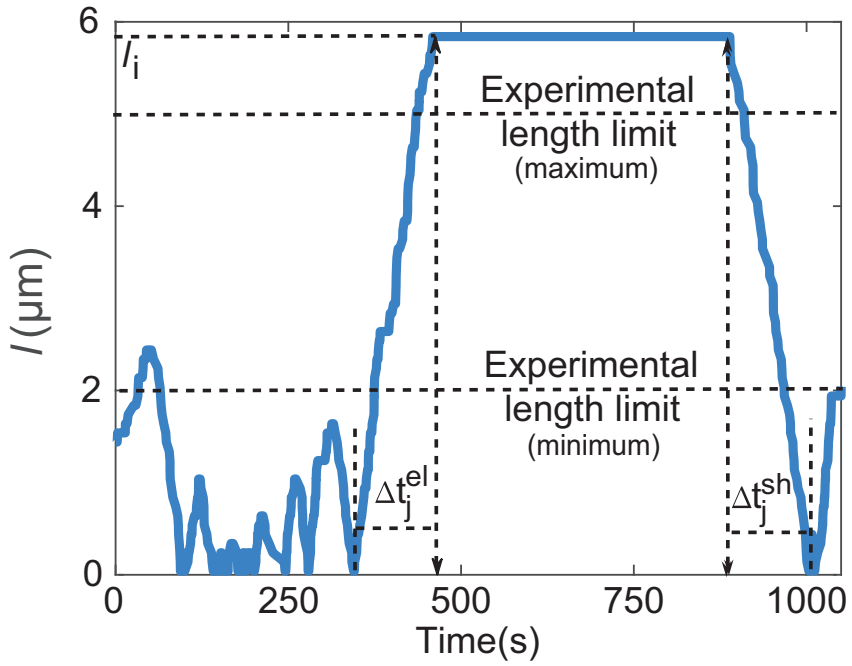

Figure S4 Microtubule dynamics and associated parameters:
Data from a typical KMC evolution of the microtubule length, l depicting the time intervals for an elongation event, Δt_j^{el} and shrinkage event, Δt_j^{sh} used while determining the elongation and shrinkage velocities. Several catastrophe events are also observed when the microtubule length reduces to zero.

3 Effect of microtubule occupancy on mitochondrial dynamics:

Occupancy of a microtubule bundle is defined as the percentage of the total time of evolution in which the predicted length of the bundle lies between the maximum and minimum length bounds observed in the experiments for the respective microtubule environment. The microtubule parameters for the selected microtubule replicate used to evaluate the mitochondrial distributions using the M1MT model are given in Table S1.

Table S1 Microtubule dynamics parameters

Microtubule type	Simulation				Experiment		
	V_{ev} (μm/s)	V_{sv} (s^{-1})	f_c (s^{-1})	Occupancy (%)	V_{ev} (μm/s)	V_{sv} (s^{-1})	f_c (s^{-1})
MT_{short}[a]	0.05	0.09	0.012	89.2	0.03[a]	0.1[a]	0.02[a]
MT_{wt}[b]	0.067	0.093	0.006	90.5	0.0425[b]	0.14[b]	0.0055[b]
MT_{long}[b]	0.04	0.065	0.001	100	0.05[b]	0.1[b]	0.00067[b]

[a]Data procured from experiments carried out for current study
[b]Represent experimentally observed parameter values [1,2]

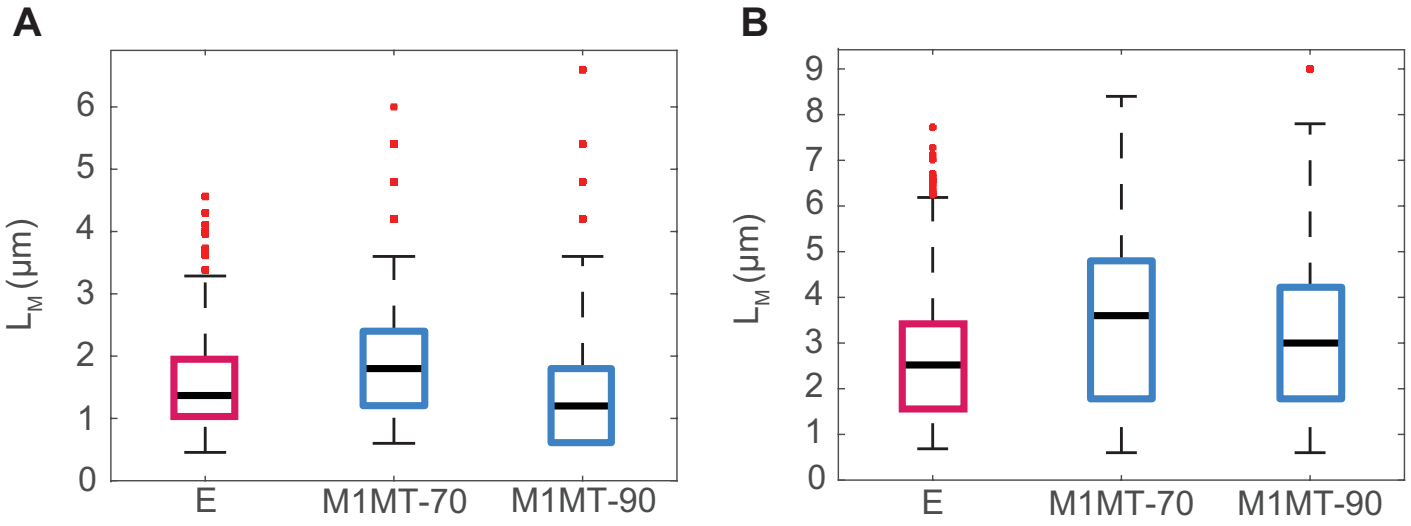

Figure S5 Effect of microtubule occupancy: Mitochondria length distribution, L_M, obtained for different percentage of occupancy of microtubules compared with experimental data (E). (A) represents data for the MT_{wt} and (B) represents data for MT_{long} environments. M1MT-70 and M1MT-90 represent the data when microtubule lengths are within experimentally observed values for 70% and 90% of the time.

4 Cell to cell variation under different microtubule environments

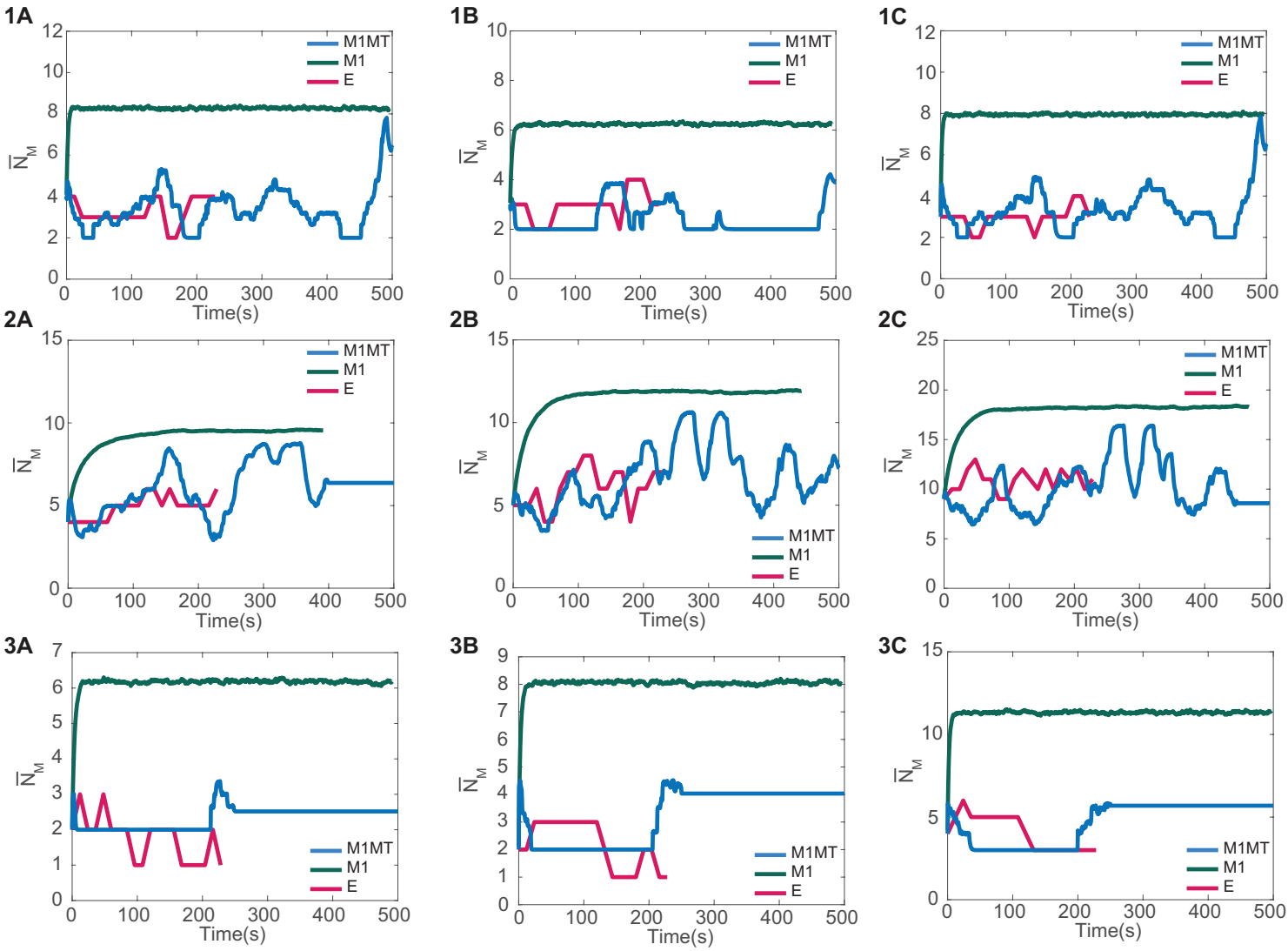

Figure S6 Comparison of models: Prediction of mitochondrial number distribution in cells having MT_{wt} (1A-1C), MT_{short} (2A-2C) and MT_{long} (3A-3C) microtubules using the M1 and M1MT models. M1 model overestimated the mean mitochondrial number roughly by a factor of 2 and M1MT model predicted a similar number distribution as observed in experiments (E). This data represents KMC evolutions for three cells for each of the different microtubule environments.

5 Microtubule mass balance

A circular cross-section of an individual microtubule consists of 13 tubulin units with a thickness of 8 nm along the long axis of the cylindrical fission yeast cell[3,4]. Using this relation between the required number of tubulin units and the length of microtubule traversed, the number of tubulin units required for 1 μm growth of a microtubule bundle consisting of 3 microtubules was computed to be 4875. The diameter of the fission yeast cell[3] was assumed to be 3.81 μm. The length of the cell was assumed to be 11.6 μm , thus considering a cylindrical geometry, the volume of the yeast cell is 132.25 μm^3 and corresponding $C_T|_{\delta x}$ for $\delta x = 0.1$ μm is 0.00614 μM.

References

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