Supplementary material for Random hydrolysis controls the dynamic instability of microtubules

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Catastrophes and rescues for arbitrary N

Catastrophes are associated with stochastic transitions between growing and shrinking dynamic phases. The microtubule is in the growing phase when it is found in one of polymer configurations with the unhydrolyzed cap of any size or when the number of already hydrolyzed monomers at the end is less than N. We define $R_{k,l}$ as a probability to be in the polymer configuration with l T monomers at the end that are preceded by k D monomers (irrespective of the state of the other subunits), $Q_{k,l}$ as a probability to be in the polymer configuration with l D monomers at the end that are preceded by k T monomers, and finally $S_{k,l}$ is a probability that the last l monomers at the end are hydrolyzed except for the one subunit at position k counting from the end of the polymer. Formally these definitions can be also written as,

$$R_{k,l} \equiv Prob(\ldots \underbrace{D \ldots D}_{k}, \underbrace{T \ldots T}_{l}), \quad Q_{k,l} \equiv Prob(\ldots \underbrace{T \ldots T}_{k}, \underbrace{D \ldots D}_{l}),$$
$$S_{k,l} \equiv Prob(\ldots \underbrace{D \ldots T \ldots D}_{l}). \tag{1}$$

Note that the probability P_l to have the unhydrolyzed cap of exactly l monomers can be expressed as $P_l = R_{1,l}$, while the probability to be found in the growing phase is

$$P_{gr} = \sum_{l=1}^{\infty} R_{1,l} + \sum_{l=1}^{N-1} Q_{1,l}. \tag{2}$$

The simple mean-field theory assumes that the state of the monomer in the microtubule is independent of its neighbors, and it also estimates that the probability to find T or D monomer k sites away from the polymer is equal to $b^{k-1}q$ or $(1 - b^{k-1}q)$ respectively, with the parameter b given by $b = \frac{U-q(W_T+r)}{U-qW_T}$. The probabilities defined in Eq. (1) can be easily calculated yielding,

$$R_{k,l} = b^{l(l-1)/2} q^l \prod_{j=l}^{l+k-1} (1 - b^j q), Q_{k,l} = b^{k(2l+k-1)/2} q^k \prod_{j=1}^{l} (1 - b^{j-1} q),$$
$$S_{k,l} = b^{k-1} q \prod_{j=1}^{k-1} (1 - b^{j-1} q) \prod_{j=k+1}^{l} (1 - b^{j-1} q). \quad (3)$$

Then the probability to be found in the growing phase is

$$P_{gr} = q + \sum_{k=1}^{N-1} b^k q \prod_{j=1}^{k} (1 - b^{j-1} q). \quad (4)$$

The frequency of catastrophes $f_c(N)$ in steady-state conditions can be found from the fact that the total flux out of the growing phase, $f_c P_{gr}$, must be equal to the flux to the shrinking phase, leading to the following equation, $f_c(N) P_{gr} = W_T R_{N,1} + r \sum_{k=1}^{N} S_{k,N}$. Using Eqs. (3) and (4), it can be shown that

$$f_c(N) = \frac{W_T \prod_{j=1}^{N} (1 - b^j q) + r \sum_{k=1}^{N} b^{k-1} \prod_{j=k+1}^{N} (1 - b^{j-1} q) \prod_{j=1}^{k-1} (1 - b^{j-1} q)}{1 + \sum_{k=1}^{N-1} b^k \prod_{j=1}^{k} (1 - b^{j-1} q)}. \quad (5)$$

For $N = 1$, we obtain a simple expression for the frequency of catastrophes, $f_c(1) = W_T(1 - bq) + r$, while for $N = 2$ it gives $f_c(2) = \frac{W_T(1-bq)(1-b^2q) + r[1-bq+b(1-q)]}{1+b(1-q)}$. A limiting behavior of the frequency of catastrophes for general N can be analyzed. For low concentrations of free GTP monomers in the solution, corresponding to $u \to 0$, we have $q \to 0$ and $b \to 1 + r/w_T$, producing $f_c(N) \simeq r + \frac{W_T}{1 + \sum_{k=1}^{N-1} (1 + r/W_T)^k}$. For large N and small hydrolysis rates ($r/W_T \ll 1$) the expression for the frequency of catastrophes is even simpler, $f_c(N) \simeq r + \frac{W_T}{N}$. Another limit of interest corresponds to large concentrations ($U \gg 1$), where $q \to 1$ and $b \to 1$, leading to $f_c(N) \to 0$ for all values of $N \geq 2$, while for $N = 1$ we have $f_c(1) \to r$.

This method of analyzing catastrophes can be also extended to calculating frequency of rescue events $f_r(N)$. The probability to find the microtubule in the shrinking phase is equal to

$$P_{sh} = 1 - P_{gr} = 1 - q - \sum_{k=1}^{N-1} b^k q \prod_{j=1}^{k} (1 - b^{j-1} q). \quad (6)$$

The total flux out of this state is given by $f_r(N)P_{sh} = UP_{sh} + W_D Q_{1,N}$, which leads to the following equation

$$f_r(N) = U + \frac{W_D b^N q \prod_{j=1}^{N}(1 - b^{j-1}q)}{1 - q - \sum_{k=1}^{N-1} b^k q \prod_{j=1}^{k}(1 - b^{j-1}q)}. \tag{7}$$

This expression can be further simplified to obtain the final result,

$$f_r(N) = U + W_D b^N q. \tag{8}$$

For all values of N in the limit of $U \to 0$ it yields $f_r \simeq U$, while for large U we have $f_r \simeq U + W_D$.

In addition, the average time before the catastrophe or before the rescue can be easily obtained by inverting the corresponding expressions for frequencies, namely, $T_c(N) = 1/f_c(N)$ and $T_r(N) = 1/f_r(N)$.