**Mathematical modelling**

**Assumptions**

The model of Ase1 accumulation on shrinking microtubules, and its effect on shrinkage speed (Fig. 4A) is built on the following assumptions:

1. The microtubule is a one-dimensional lattice, where lattice of size =8nm start at index at the plus end, extending to .
2. Only bound Ase1 molecules are considered by recording the presence or absence (0 or 1) of Ase1 in each lattice site. Bound Ase1 molecules exchange with solution with two constant rates (). Binding is only allowed if the lattice site is empty (Fig. 4A). was directly measured, and was adjusted to match the Ase1 equilibrium density on microtubules (Table S1).
3. Ase1 particles on the lattice undergo unbiased diffusion characterized by a constant hopping rate (). Hopping is only allowed to an empty site (Fig. 4A). The rate is calculated from the experimentally measured diffusion coefficient of Ase1 (Table S1), as .
4. The Ase1 particle in the terminal site (), cannot hop past the microtubule end (red arrow on the left of Fig. 4A), but can detach with rate .
5. The terminal lattice site may dissociate from the microtubule, with rate which depends on the presence of Ase1, according to each model:
   1. In Model 1, it occurs with rate if the terminal lattice site is not occupied (Fig. 4B top), and with rate if it is occupied (Fig. 4B bottom). is a parameter between zero and one. If , the presence of Ase1 has no effect, and if , the first tubulin subunit cannot unbind if it is bound to Ase1.
   2. In Model 2, it occurs with rate if the first lattice sites are all not occupied (Fig. 4C top), and with rate if any of the terminal sites is occupied (Fig. 4C bottom).
   3. For Model 3 (phenomenological model) see below.

is derived from the depolymerization rate of microtubules in the absence of Ase1 (), measured experimentally (Table S1), such that .

1. If the terminal lattice site dissociates when a molecule of Ase1 is bound to it, this Ase1 is lost as well (Fig. 4B, bottom).

**Simplification to a system of constant size**

Since terminal subunits are more likely to be lost when they are without Ase1 than when they are with Ase1, any dissociation event increases the density of Ase1 remaining on the microtubule. This effect is only present at the microtubule tip, and away from the tip, the probability of a binding site being occupied is only determined by the binding and unbinding constants: .

Therefore, we can restrict the model to a section of the microtubule with lattice sites, as long as the probability of finding a molecule at position is close to . When a depolymerisation event happens, we shift the lattice indexes such that site becomes site , and set .

**Mean field theory**

The system can be solved using a mean-field approximation, by just considering the ensemble of , the average probability of a site being occupied and neglecting higher-order correlations between neighbouring sites. We can then write a set of discrete differential equations to represent the dynamics of the system:

Specific equations apply at the boundaries and :

The terms of the equation are associated with the rates of diffusion, binding, unbinding () which are constant, and the depolymerization rate (), which is affected by lattice occupancy in a different way in each model (see Assumptions).

For Model 1, .

For Model 2, .

This dynamical system can be evolved from any initial conditions, converging to the unique steady-state solution for a set of given parameters. Assuming that the microtubule is at binding equilibrium when it starts shrinking, we initially set for all sites. From those initial conditions, we integrate the equations numerically using Python’s *odeint* function (see source code).

**Phenomenological model**

The third model is phenomenological because it considers multiple protofilaments without including their true spatial arrangements. In this model, we use the same equations as before, except for . The key simplification is to assume that all protofilaments are in register and that the probabilities for different protofilaments are all equal for any . With this simplification the system of equations is easily solvable, capturing the effect that cooperativity across protofilaments might have on shrinkage speed. A geometrically more realistic model is possible but out of scope of the current study.