**Mathematical modelling**

**Assumptions**

To model the accumulation of Ase1 on shrinking microtubules, and its effect on growth speed (Fig. 4A), we make the following assumptions:

1. We treat the microtubule as a one-dimensional lattice, where lattice index is 1 at the plus end, and the size of lattice units is =8nm, corresponding to the size of a tubulin dimer.
2. We assume a constant concentration of Ase1 molecules in solution. Therefore, Ase1 molecules are represented as particles that can bind and unbind to a lattice site with 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 X).
3. Bound Ase1 molecules undergo unbiased diffusion on the lattice with constant hopping rates (). Diffusion is only allowed if the target site is empty (Fig. 4A). The rate is derived from the diffusion coefficient of Ase1 () calculated experimentally (Table X), such that .
4. When diffusing, if Ase1 reaches the microtubule end, it does not detach (red arrow on the left of Fig. 4A).
5. The first lattice site may detach from the lattice, with rate which depends on the presence of Ase1, and is different for each model:
   1. In Model 1, it occurs with rate if the first lattice site is not occupied (Fig. 4B top), and with rate if the plus end is occupied (Fig. 4B bottom). is a parameter that goes from zero to 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 not occupied (Fig. 4C top), and with rate if either of the first 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 X), such that .

1. If a molecule of Ase1 is bound to the first lattice site when the lattice site detaches, that Ase1 detaches from the lattice as well (Fig. 4B, bottom).

**Simplification to a system of constant size**

Since subunits without Ase1 are more likely to be lost at the plus-end, depolymerization increases the density of Ase1 at the shrinking end. However, in the microtubule body, where the boundary effect of the plus end dissipates, the probability of a binding site being occupied tends to , which is solely determined by the binding and unbinding constants.

Therefore, we can model only a fraction of the microtubule with lattice sites, as long as the probability of finding a molecule at position tends to . When a depolymerisation event happens, we can shift the lattice indexes such that site becomes site . The probability of the newly added site being occupied is .

**Mean field theory**

To study the behavior of such a system, we use a mean-field approach where we consider the average probability of a site being occupied, and neglect correlations between neighbouring sites. We can then write a discrete differential equation of the probability of a site being occupied in the bulk of the microtubule:

Separate equations govern the change in density at sites 1 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 system of differential equations can be evolved from any initial conditions, and always converges to the same solution for a set of given parameters. To study the dynamics of the system by evolving the equation, we assume that the microtubule is at binding equilibrium when it starts shrinking, and initially set the probability of all the lattice sites to . From those initial conditions, we integrate the equations numerically using Python’s *odeint* function (see source code).

**Phenomenological model**

We used a phenomenological model (Model 3) to explore the possibility of Ase1 molecules in neighboring protofilaments also affecting the unbinding rate of the first lattice subunit. In this model, we use the same equations as before, except for . This is an oversimplification and would be equivalent to assuming that all protofilaments are in register and that the probability of sites being occupied would be equal. Nevertheless, it allows to capture the effect that cooperativity across protofilaments may have on shrinkage speed without having to account for the complexity of a multi-protofilament model.