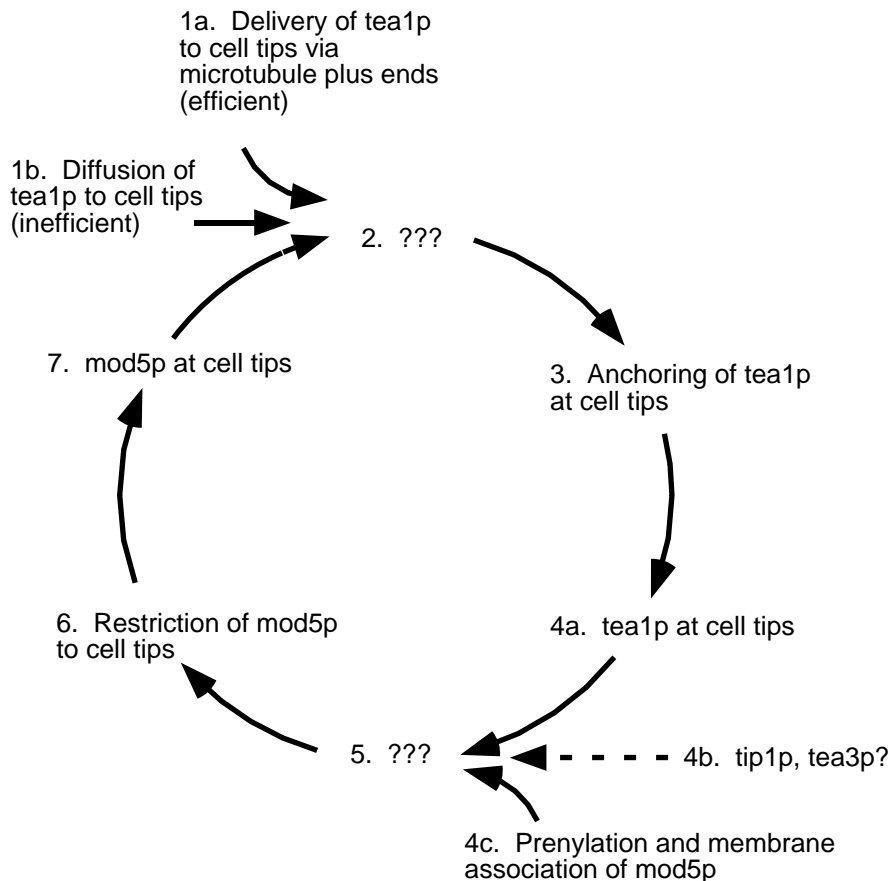


Formal structure of a positive feedback loop in which mod5p and tea1p regulate each other's localisation.



Question marks at critical points indicate that the mechanisms (and timing) of this regulation are not clear. Initially (1a) tea1p is delivered to cell tips by association with microtubule plus ends; our polarity re-establishment experiments in the presence of MBC suggest that tea1p can also reach cell tips in the absence of microtubules, albeit less efficiently (1b; see Fig. 2). The presence of mod5p at cell tips (7) leads to the anchoring of tea1p at cell tips (3), by a yet-unknown mechanism (2). Having tea1p at cell tips (4a) ultimately leads to restriction of mod5p membrane-localisation to cell tips (6), and mod5p membrane-localisation itself requires the C-terminal prenylation motif of mod5p (4c; see Fig. 4). The mechanism by which tea1p restricts mod5p localisation is unclear (5), but may involve tip1p, and possibly tea3p (4b), as mutations in these genes lead to a reduction in mod5p at cell tips (see Suppl. Fig. 8). Although *tip1* mutants have short microtubules and therefore aberrant targeting of tea1p to cell tips, this alone would not explain the defects in mod5p localisation seen in *tip1* mutants, because low amounts of tea1p are nevertheless detected at cell tips in *tip1* mutants (see Suppl. Fig. 10), and *tea2-1* mutants, which have a similar phenotype to *tip1* mutants with respect to microtubule organisation and tea1p localisation, do not show a similar defect in mod5p localisation (see Suppl. Figs 8-10). We have also shown that sudden (but incomplete) loss of tea1p from cell tips after microtubule disruption leads to a partial relaxation of the restriction of mod5p to cell tips (see Suppl. Fig. 6); this would be consistent with a model in which continuous feedback throughout the cell cycle is required for co-maintenance of tea1p and mod5p localisation. However, it is equally possible that some aspects of regulation might function at critical points in the cell cycle, and/or that tea1p and mod5p have different rates of turnover at cell tips.