A mathematical model of MAP2 dependent elongation and branching in growing dendrites

Abstract for FENS, Lisbon, July 2004

Gregor A. Kiddie, Arjen van Ooyen and Bruce P. Graham

The growth of a neuronal dendritic tree depends on the neuron's internal state and the environment within which it is situated. Different types of neuron develop dendritic trees with specific characteristics, such as the average number of terminal branches and the average length of terminal and intermediate segments. A key aspect of the growth process is the construction of the microtubule cytoskeleton within the dendritic tree. Neurite elongation requires assembly of microtubules from free tubulin at the growth cone. The stability of microtubule bundles is an important factor in determining how likely it is for a growth cone to split to form new daughter branches. Microtubule assembly rates and bundle stability are controlled by microtubule-associated proteins, principally MAP2 in dendrites. Extending our previous work (Hely et al, J. Theor. Biol. 210:375-384, 2001) we have developed a mathematical model of neurite outgrowth in which elongation and branching rates are determined by the phosphorylation state of MAP2 at the tips of each terminal branch. Tubulin and MAP2 are produced in the cell body and transported along the neurite by a combination of diffusion and active transport. Microtubule (dis)assembly at neurite tips is a function of tubulin concentration. The rate of assembly depends on the amount of unphosphorylated MAP2 bound to the microtubules and linking them together. Phosphorylation of MAP2 destroys its linking capability and destabilises the microtubule bundles. Each terminal has a probability of branching that depends on the phosphorylation of MAP2 which, in turn, is a function of calcium concentration. Initial results from this model show that changes in the (de)phosphorylation rates of MAP2 affect the topology of the final dendritic tree. Higher phosphorylation promotes branching and results in trees with many short terminal branches and relatively long intermediate segments. Reducing phosphorylation promotes elongation and inhibits branching.