

Mathematical model of self-organizing and adaptable intracellular transport network

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Last decade investigations proved the importance of microtubules in viral entry into cell, atherosclerosis development, cancer therapy and nervous system diseases. Our aim is to reconstruct mechanisms that form intracellular transport network capable of adaptive changes of cellular metabolic state. We constructed a mathematical model of intracellular microtubular transport system self-organization and cargo transfer, which is an extension of the model of microtubule self-organization in melanophores [1].

Our model is a combination of two coupled blocks: agent-based and continuous ones. Agent-based block directly simulate individual microtubule dynamics: nucleation (new microtubule birth), polymerization, depolymerization and death. Individual microtubule end dynamics and stabilization factors result in transport network formation and this process is called self-organization. The general feature of transport network is defined by localization of nucleation centers and membrane, which microtubule plus-ends are stabilized on. Continuous block embodied by partial differential equation describing cargo transfer along microtubule network, initial and boundary conditions that describe endocytosis (positive flux) or zero flux through the cell membrane. The model was implemented with finite volumes method and direct simulations.

We simulated the experiment on intracellular endosome transport described in [2] and obtained the patterns similar to the original experiment that are positive correlation between total number of endosomes and mean distance from nucleus to endosomes, negative correlation between mean endosome size and total number of endosomes, negative correlation between mean endosome size and mean distance from nucleus. However, the mechanism of endosome size dynamics has been studied insufficiently. Thus we included an assumption of continuous endosome size decrease. This assumption is based on a functional link between endosome size and its distance from nucleus [2].

We also obtained general shape of multisection transport network with symmetric microtubule spatial distribution. We currently consider the factors that influence microtubule stability and growth direction choice. These factors result in preferable directions of microtubules in transport network in the living cell.

1. E. N. Cytrynbaum, V. Rodionov, A. Mogilner (2004) Computational model of dynein-dependent self-organization of microtubule asters, *Journal of Cell Science*, **117**: 1381–1397.
2. C. Collinet et al. (2010) Systems survey of endocytosis by multiparametric image analysis, *Nature*, **464**:243–249
3. K.A. Novikov, A.N. Gratchev, J.G. Kzhyshkowska, O.A. Melnichenko, A.A. Romanyukha (submitted to publication) Mathematical model of intracellular vesicular transport over tubulin cytoskeleton, *Mathematical Models and Computer Simulations*.