Mathematical model and software FRAPAnalyser for analysis of actin-cytoskeleton dynamics with FRAP experiments

A. Halavatyi, S. Medves, C. Hoffman, V. Apanasovich, M.Yatskou, E. Friederich.
Proceedings of FEBS/ECF Workshop "Mechanics and dynamics of the cytoskeleton" 22nd -26th June, 2008, Potsdam, Germany, p.50.

A novel mathematical model describing actin dynamics in living cells under steady-state conditions has been developed. Conversely to other models which use average lifetime of actins in filaments and actin turnover rate as parameters of the actin polymerization process, our model operates with unbiased actin association/dissociation rate constants and takes into account filament length. The model formalism assumes reaction dominant regime, a uniform concentration of actin filaments and bleached actin subunit diffusivity due to the association/dissociation processes at the filaments ends. The spatiotemporal evaluation of fluorescent actin population is described by a system of stochastic equations. The model parameters include the average length of filaments, the association/dissociation rate constants, the initial distribution of bleached actins in filaments. The model was validated on synthetic theoretical data generated by a stochastic simulation model utilising the Gillespie's algorithm. Results show that: i) the kinetics of FRAP recovery for bleached actin filaments depends on reaction rate constants for barbed and pointed ends, length and concentration of filaments; ii) size of the bleach spot merely influences the fluorescence recovery if filaments are organised anisotropically. This model was applied for FRAP analysis of focal adhesion protein Tes in Vero cells. Importantly, we provide a free software package FRAP Analyser integrating the developed model and other widely-used FRAP fitting models.

An automated integrative computer simulation approach for stochastic modelling of actin-polymerization

M. Yatskou , A. Halavatyi, P. Nazarov, S. Medves, M.van Troys, C. Ampe, E.Friederich
Proceedings of FEBS/ECF Workshop "Mechanics and dynamics of the cytoskeleton" 22nd -26th June, 2008, Potsdam, Germany, p.100.

We report an automated universal approach for advanced modelling of actin polymerization processes, integrated into a stand-alone software package, which offers a broad application panel. The simulation package integrates major actin-related reactions, such as assembly of actin nuclei, association/dissociation of monomers to filament ends, ATP-hydrolysis and ADP-ATP exchange via ADP-Pi formation, branching, severing, annealing and the effects of regulatory proteins. These biochemical reactions are linked to information on the structure of filaments, the nucleotide compositions of actin monomers and of actin subunits in filaments and to filament aging (ATP hydrolysis). Several modelling algorithms were updated and compared, in particular, the Gillespie's "direct" method and its modifications: the first reaction method, the "next reaction" method of Gibson-Bruck and the τ-leap algorithm. The developed Monte Carlo modelling schemes were validated on: i) synthetic theoretical data generated by an analytical model and ii) sets of our and published experimental data obtained from fluorescence pyrene-actin experiments. The designed model can be extended for predictive evaluation of the activities of other actin-interacting proteins and can be applied for the analysis of experimental pyrene actin-based or fluorescence microscopy data. We provide a free software package *ActinSimChem* that integrates the developed simulation algorithms.