3rd grade: Spatio-temporal model of NF-κB oscillation

Summary: The pathway model is the same as in "3rd grade: Oscillation of transcription factor NF-κB". To construct spatio-temporal model of NF-κB oscillation, reactions are simply embedded to corresponding region in the 3D shape of a cell. Therefore, here we describe the embedding of reactions.

Construction of 4D A-Cell model

First 3D spherical shape is constructed in A-Cell followed by the regional segregation of the nucleus as shown in the center of Fig.1. The diameter of a spherical cell model is 50 μm, which is divided into 31 compartments in the radial direction. The nucleus is located at the center with 13 compartments in its radial direction. The outermost compartments of the nucleus are defined as the nuclear envelope, where import and export reactions are embedded.

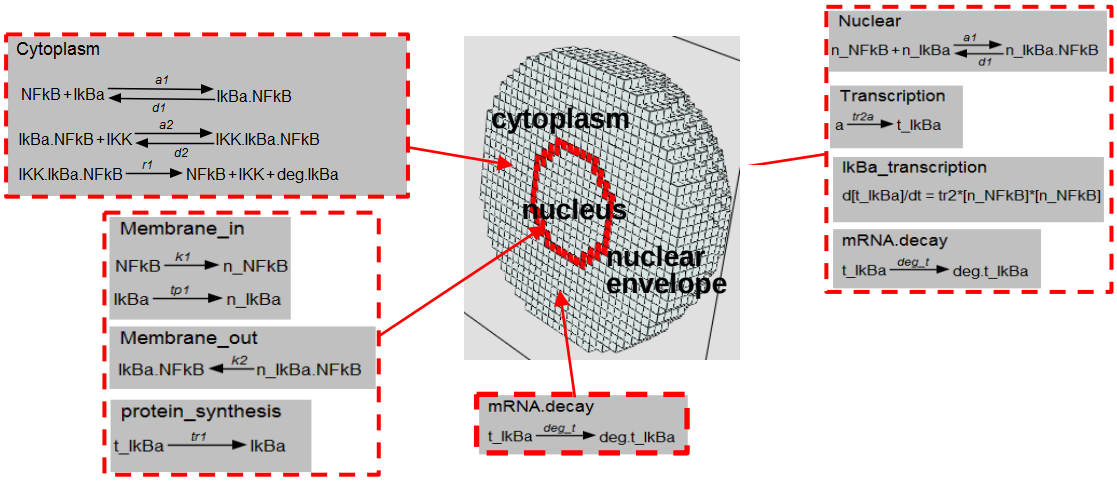

Fig.1 Embedding reactions to 3D spherical shape for 4D spatio-temporal simulation

Thus the construction of 4D simulation model is easily realized by using A-Cell. Running simulation is also easy (Cf. "Introduction to A-Cell" and "A-Cell Operation Manual"). The main difficulties lay in the analyses of the simulation results: why NF-κB oscillates, and what regulates the oscillation pattern. Although these are beyond the scope of this document, we would like to point out one important simulation result. Parameters (rate constants) for pathway simulation that reproduce experimental observation do not reproduce observation in 4D simulation (Fig.2). Thus, a parameter set in realistic simulation should be changed from that in non-realistic simulation.

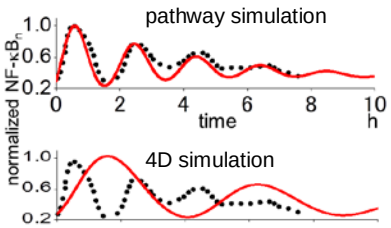

Fig.2 Experimental observation is not reproduced by a parameter set used in the pathway simulation that has no spatial extent. Thus, parameter set in pathway simulation should be changed. Dots: experiment, and red lines: simulations.

Reference: Ohshima, D., et al., PLoS ONE., 7(10): e46911.