A single cell simulator to interpret dynamics of protein trafficking and transport

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A novel cell simulator as an analyzing tool of dynamic protein expression and spatial translocation at the cellular level is proposed in this study. The cell simulator provides qualitative and quantitative information for the intracellular dynamics of proteins by creating a reconstructed cell model then solving stochastic equations with event-based stochastic simulation for protein syntheses and transport in a single astrocyte cell. In the aquaporin 4 regulation, sulforaphane administration increases the translocation of the transcription factor, Nrf2, into the nucleus, which activates the aquaporin 4 gene to transcribe mRNA. Gillespie based discrete time approximation method results in stochastic fluctuation of mRNA and aquaporin 4 molecules, and is ideal for representing gene transcription events in a single cell. Computations predict AQP4 upregulation to be 68% after 18 hours of sulforaphane treatment and the experiment of aquaporin 4 expression with western blotting and immunofluorescence of cultured primary astrocytes agree well with the model prediction. The demonstrated cell simulator offers the seamless integration of experimental data with mathematical modeling of systems biology.