An in silico approach to analyzing FRAP recovery curves in nuclei using an extension of the Gillespie algorithm.

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Our motivation is to analyze the diffusion of proteins within an environment where spatial in-homogeneity plays a crucial role, such as in the cell nucleus. We have developed a new computational approach using the ReDi (reaction diffusion) program, aimed at quantifying protein diffusion due to Brownian motion in cellular processes.

To better understand the role of geometric elements, including chromatin fibers, diffusing volumetric molecules and other proteinaceous bodies, upon proteins as they diffuse into the bleached regions, we compared our results to experimental data.

Here, we applied our process to FRAP recovery curves, established by photobleaching a thin band in a cell and measuring signal recovery over time. Utilizing an extension of the Gillespie algorithm, simulations were run using an idealized nucleus (5 microns per side) of roughly spherical shape, divided into 64,000 cubic elements (Bernstein et al. 2006).
Utilizing a discrete in silico approach allowed us to more accurately analyze parameters such as initial protein concentrations, diffusion coefficients, binding affinities, in quantifying these recovery curves.

We report on our FRAP error analysis introduced when the area of a bleached regions width changes. We adjust the bleached area and quantify discrepancies in recovery as compared to experimental data, illustrating the error inherent to current analytical techniques.

By accounting for such critical elements as nuclear topology, protein size and concentration, cellular 3-dimensionality, we offer an improved method to analyzing diffusion dependent processes in cells.

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