A Quantitative Kinetic Model for the in Vitro Assembly of Intermediate Filaments from Tetrameric Vimentin

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In vitro assembly of intermediate filament proteins is a very rapid process. It starts without significant delay by lateral association of tetramer complexes into unit-length filaments (ULFs) after raising the ionic strength from low salt to physiological conditions (100 mM KCl). We employed electron and scanning force microscopy complemented by mathematical modeling to investigate the kinetics of in vitro assembly of human recombinant vimentin. From the average length distributions of the resulting filaments measured at increasing assembly times we simulated filament assembly and estimated specific reaction rate parameters. We modeled eight different potential pathways for vimentin filament elongation. Comparing the numerical with the experimental data we conclude that a two-step mechanism involving rapid formation of ULFs followed by ULF and filament annealing is the most robust scenario for vimentin assembly. These findings agree with the first two steps of the previously proposed three-step assembly model (Herrmann, H., and Aebi, U. (1998) Curr. Opin. Struct. Biol. 8, 177 - 185). In particular, our modeling clearly demonstrates that end-to-end annealing of ULFs and filaments is obligatory for forming long filaments, whereas tetramer addition to filament ends does not contribute significantly to filament elongation.

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