Supporting Material for:

Soluble protofibrils are metastable intermediates in simulations of amyloid fibril degradation induced by lipid vesicles

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November 26, 2009

Supplementary Figures

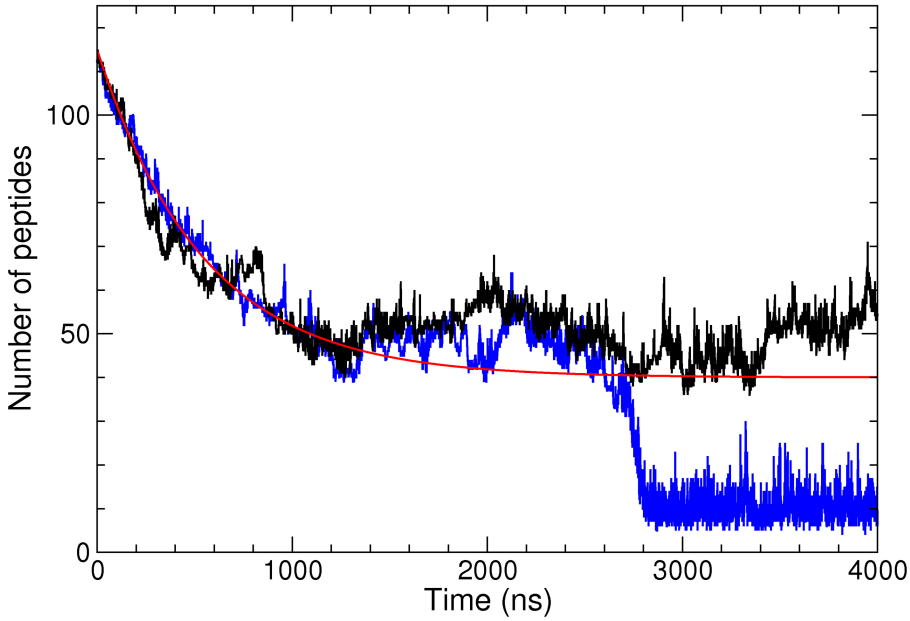

Figure 1: Kinetics of fibril disaggregation. The size of the largest peptide aggregate is shown as a function of the simulation time for two simulations of 4PF2 fibril disaggregation, one in which the fibril fully disaggregates (blue) and one in which it does not (black). The initial phase of both simulations can be fitted to a first order decay process (red line): $N_t = (N_0 - N_s)e^{-\lambda t} + N_s$ where N_t, N_0 and N_s are the number of peptides that form the largest aggregate at time t, at the beginning of the simulation and in a steady state, respectively. λ is a rate constant. At the second disaggregation phase (corresponding to oligomer disintegration), observed here only for the simulation depicted in blue, disaggregation is fast and the rate is linear with time.

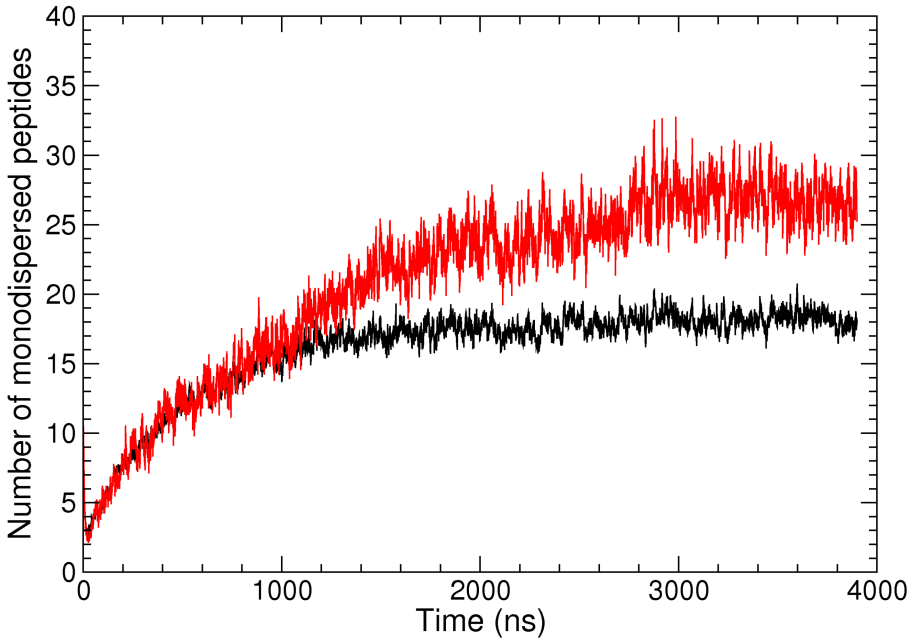

Figure 2: The number of peptide monomers in the bulk increases during the simulations of disaggregation, and the high concentration in the bulk stabilizes the backward oligomers. The average number of monomers in the bulk is shown for 38 simulations of the 4PF2 fibrils (black) and only for the subset of nine simulations where the fibrils underwent complete degradation (red).

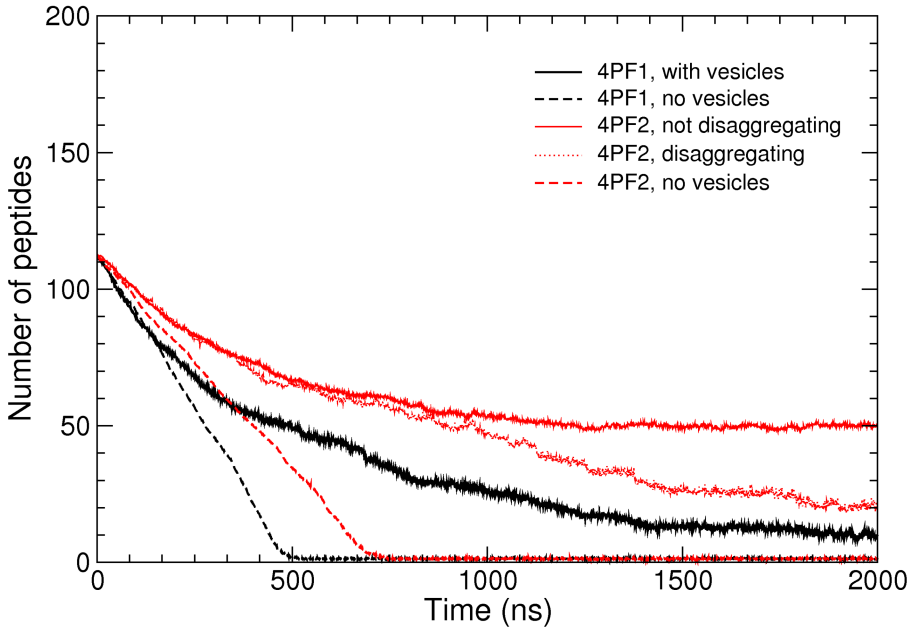

Figure 3: Disaggregation of fibrils with different morphologies. The average number of peptides in the largest aggregate is shown as a function of the simulation time for fibrils of two morphologies (4PF1 and 4PF2, shown in black and red, respectively). Solid lines correspond to simulations in the presence of a vesicle. Note that the end-state after 2μs is monomeric in the first case and oligomeric in the second case. Red dotted line refers to ten 4PF2 simulations where disaggregation was observed. Dashed lines correspond to simulations in the absence of a vesicle and in a larger box, whose volume is 30 times that of the box in the simulations with the vesicle. Note the difference in kinetics between the simulations in the presence of the vesicle or at high dilution.