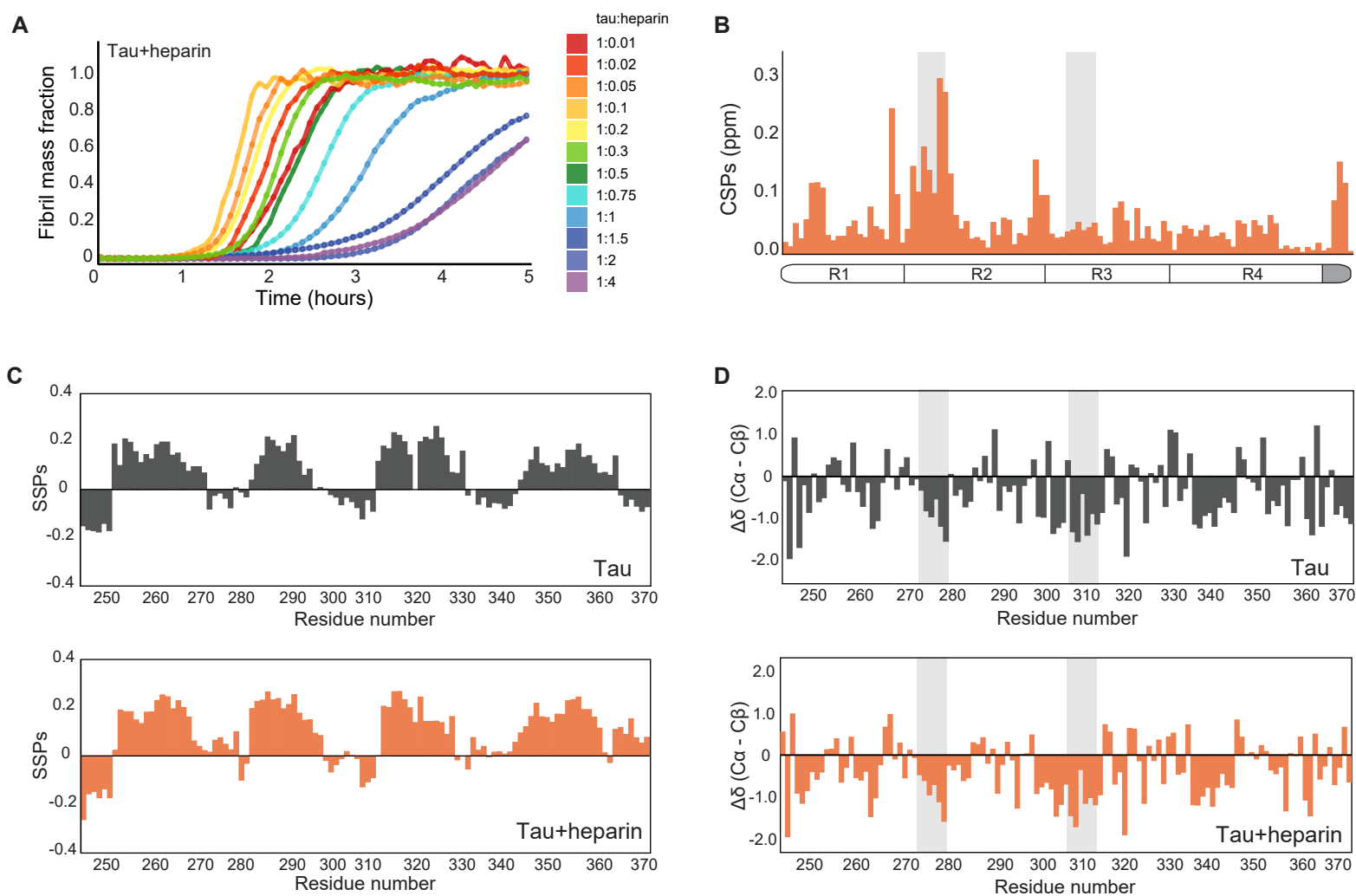


Figure 4 – figure supplement 1



**Characterization of heparin-bound tau. (A)** Tau aggregation profiles in the presence of increasing concentrations of heparin ranging from 0.1 to 40  $\mu$ M. Initially, the rate of aggregation increases with the concentration of heparin. At 1  $\mu$ M heparin, the reaction slows, with higher concentrations (20-40  $\mu$ M) suppressing aggregation completely for over 2 hours (dark blue to purple curves). **(B)** Chemical shift perturbation plot of tau upon addition of 2-fold excess of heparin. Heparin binding occurs mainly in repeat 2 (R2) of tau. The grey boxes represent tau PHF6\* and PHF6 aggregation-prone motifs. **(C)** Secondary structure propensity plot (51) of monomeric tau (black, top) and tau-heparin complex (orange, bottom). **(D)** Differences between secondary chemical shifts of C $\alpha$  and C $\beta$  resonances relative to their random coil shift (69) as a function of residue number for tau (grey) or tau-heparin complex (orange).