Supporting Information

Catalytic prion-like cross-talk between a key Alzheimer's disease Tau-fragment R3 and the Type 2 diabetes peptide IAPP

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Ion-mobility measurements

The drift cell consists of two components, a uniform low electric field that pulls the ions through the cell and buffer gas that collides with the ions and slows their motion. If both the electric field and buffer gas pressure are constant throughout the drift cell, ions drift with a constant velocity, v_d;

$$v_d = K.E \quad (1)$$

where E is the electric field strength and is dependent on both the cell length (L) and the voltage (V) applied across the cell. K is the proportionality constant that corresponds to ion mobility, which is typically expressed as the reduced mobility K_0.

$$E = \frac{V}{L} \qquad K_0 = K\frac{P}{760}\frac{273}{T} \qquad (2)$$

P is the pressure in Torr and T is the temperature in Kelvin. Equations (1) and (2) can be combined to give Eqn (3);

$$v_d = \frac{L}{t_d} = K.E \quad t_d = t_a - t_0 = \frac{L}{K.E} = \frac{L^2}{K_0(760)}\frac{(273)P}{T}\frac{}{V} \qquad (3)$$

where t_a is the ion's arrival time at the detector, t_d is the drift time through the cell and t_0 is the time outside the drift cell. The reduced mobility K_0 is influenced by both ion and buffer gas surface area and mass. Therefore, it is directly related to the collision cross-section of the analyte (σ);

$$K_0 = \left(\frac{3e}{16N_0}\right)\left(\frac{2\pi}{\mu k_B T}\right)^{1/2}\frac{1}{\sigma} \qquad (4)$$

where N_0 is the buffer gas number density, e is the charge on the ion, μ is the ion and buffer gas reduced mass, and k_B is the Boltzmann constant.

Arrival time distribution fitting

The flux of mass selected ions exiting the drift cell is used to generate theoretical arrival time distribution (ATD) fits, which are utilized to interpret our experimental ATDs. Assuming that no ion is generated or lost due to reactions with the helium buffer gas within the drift region, the ion flux exiting the drift cell can be modeled as a series of periodic delta-function packets that comprise ATD peaks.[1]

$$\Phi(0,z,t) = \frac{sa}{4(\pi D_L t)^{1/2}}\left(v_d + \frac{z}{t}\right) \times \left[1 - \exp\left(-\frac{r_0^2}{4D_T t}\right)\right]\exp\left[-\frac{(z - v_d)^2}{4D_L t}\right] \quad (5)$$

where z is the drift distance, t is drift time, s is the source packet density, a is the exit aperture area, r_0 is the radius of the initial ion packet, D_L and D_T are the longitudinal and transverse diffusion coefficients, and v_d is the drift velocity. The theoretical line shape generated from Eqn 5 corresponds to an ion packet composed of a single conformation. If the experimental line shape is broader than the theoretical line shape, this indicates that more than one conformation/oligomer is generating the experimental peak.

Supporting Figure 1

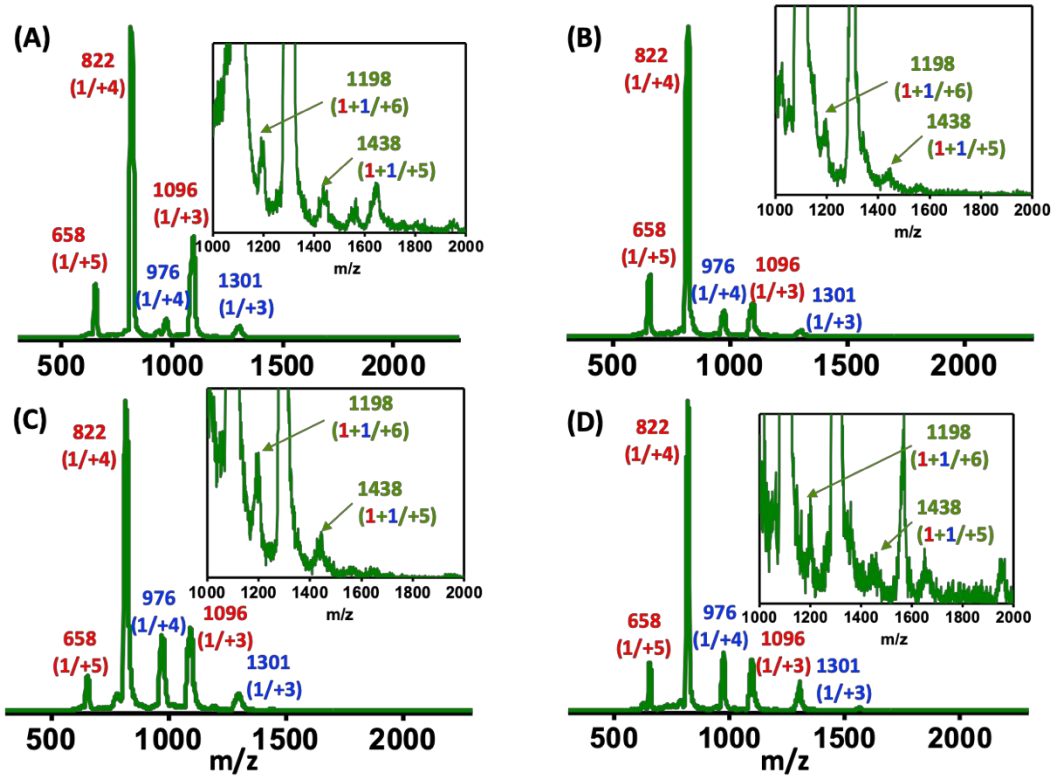

Figure S1. The mass spectra for R3-IAPP mixtures at different R3 and IAPP concentrations. (A) 150μM Tau R3 and 50μM IAPP (3:1 R3:IAPP), (B) 100μM Tau R3 and 50μM IAPP (2:1 R3:IAPP), (C) 75μM Tau R3 and 75μM IAPP (1:1 R3:IAPP), and (D) 50μM Tau R3 and 50μM IAPP (1:1 R3:IAPP). The signature peaks for IAPP and Tau are shown in blue and red, respectively. The peaks that correspond to hetero-oligomers were observed at all concentrations and are shown in the inset.

Supporting Figure 2

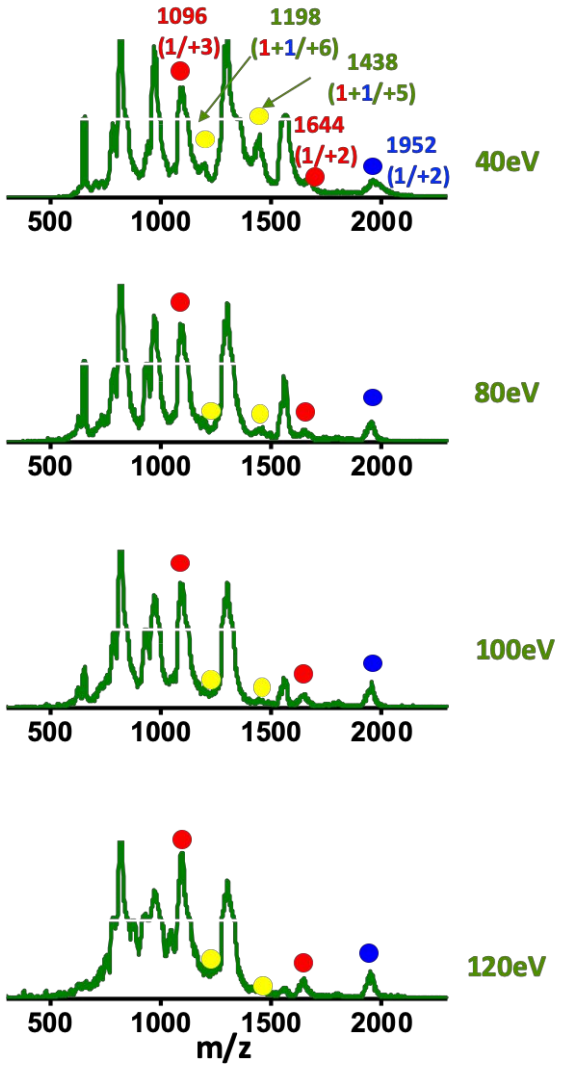

Figure S2. The mass spectra of the 1:1 mixture of IAPP (100 μM) and Tau R3 (100 μM) at increasing drift cell injection energies as shown in Figure 1B, with additional peaks that are not shown in Figure 1B. With an increase in injection energy, a drop in the relative contribution of hetero-oligomer peaks and an increase in the peaks of IAPP (1/+2) and Tau R3 (1/+2 and 1/+3) monomers was observed. This is indicative of hetero-oligomers dissociating into IAPP and R3 monomers. The increase in the signal for Tau R3 (1/+2) has also been shown in Figure 1B.

Supporting Figure 3

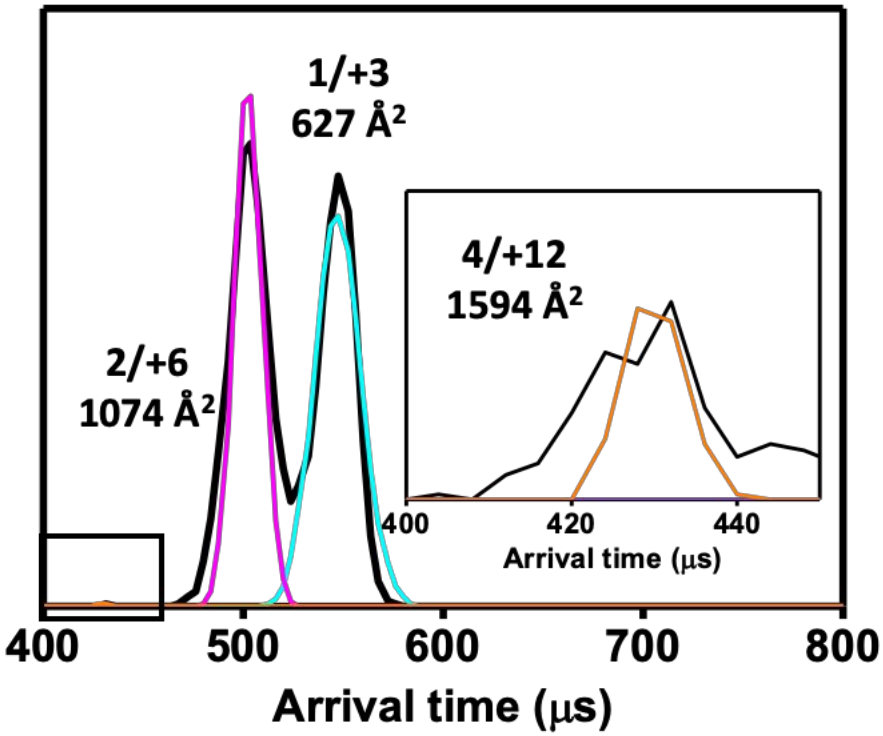

Figure S3. The arrival time distributions (ATD) for +3 charge state of Tau R3 (m/z ~1096) in a 1:1 mixture with IAPP showing the formation of tetramer (in the inset) along with monomer and dimer. The concentration of both peptides in the mixture was 100 μM. The raw data is shown in black and the fitted peaks are shown in color (cyan, pink, and orange). The procedure for peak fitting is described above.

Supporting Figure 4

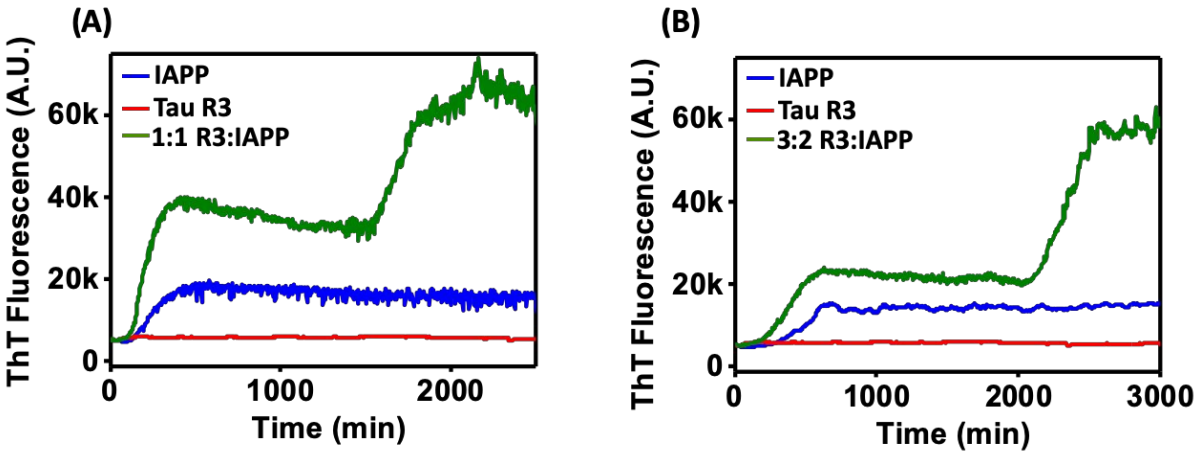

Figure S4. Thioflavin T (ThT) fluorescence data for IAPP (blue), Tau R3 (red) and mixture of IAPP and Tau R3 (olive): (A) 1:1 R3:IAPP and (B) 3:2 R3:IAPP. The samples were incubated at 37°C in the plate reader and were continuously stirred without NaCl. The concentration of Tau R3 was 75 μM and the concentration of IAPP was 75 μM and 50 μM in 1:1 and 3:2 mixture, respectively. The concentration of ThT was 50 μM in all samples. The IAPP used for this experiment was purchased from Aapptec.

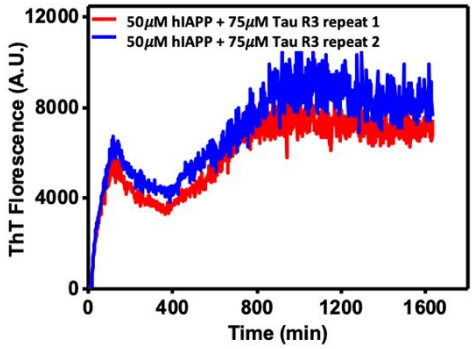

Figure S5. Two replicates of ThT fluorescence data for a 3:2 Tau:IAPP mixture is shown. The mixture was incubated at 37°C in the plate reader and was continuously stirred with NaCl. The concentration of ThT was 50 μM, the concentration of Tau R3 was 75 μM and the concentration of IAPP was 50 μM.

Reference:

1. E. A. Mason, E. W. McDaniel; Wiley: New York, 1988.