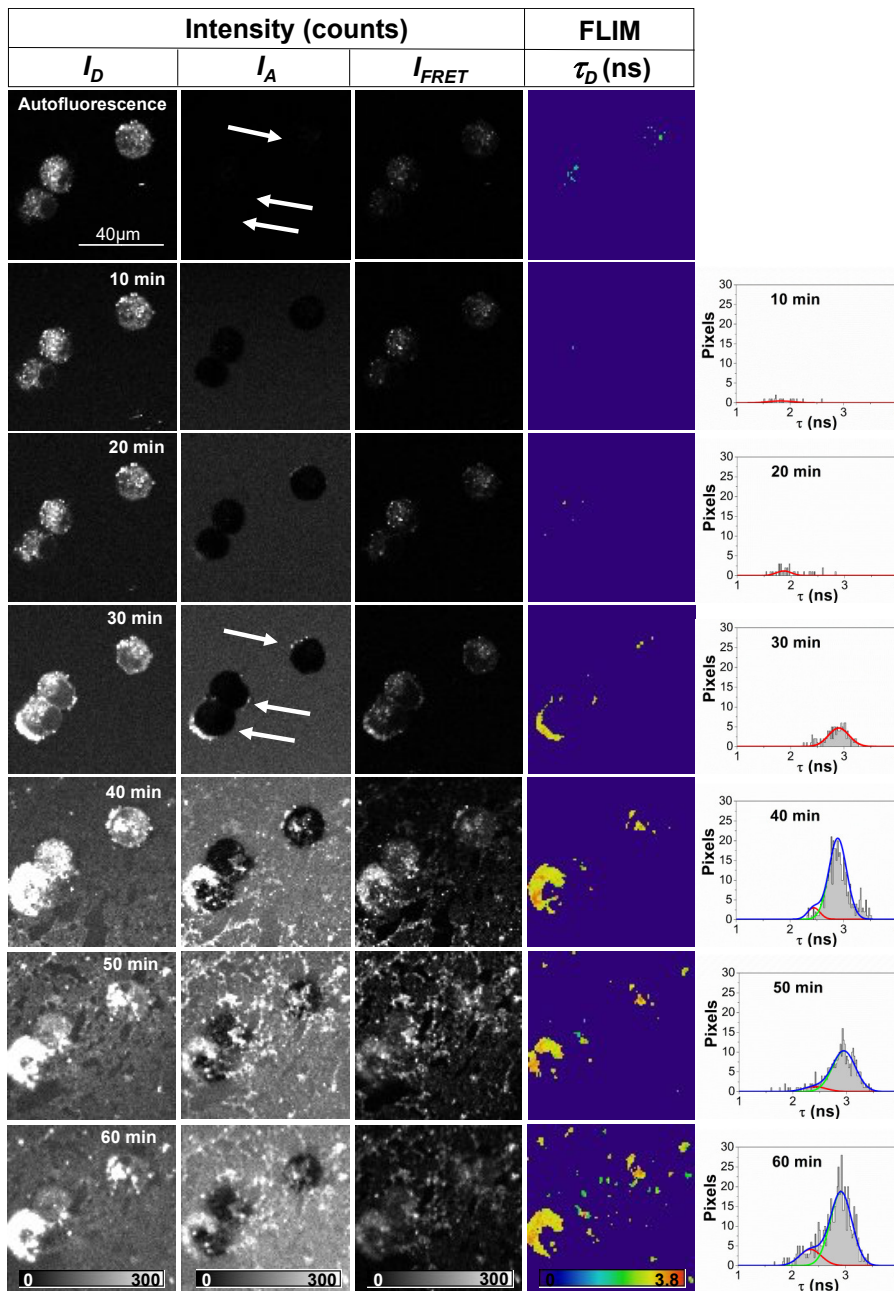


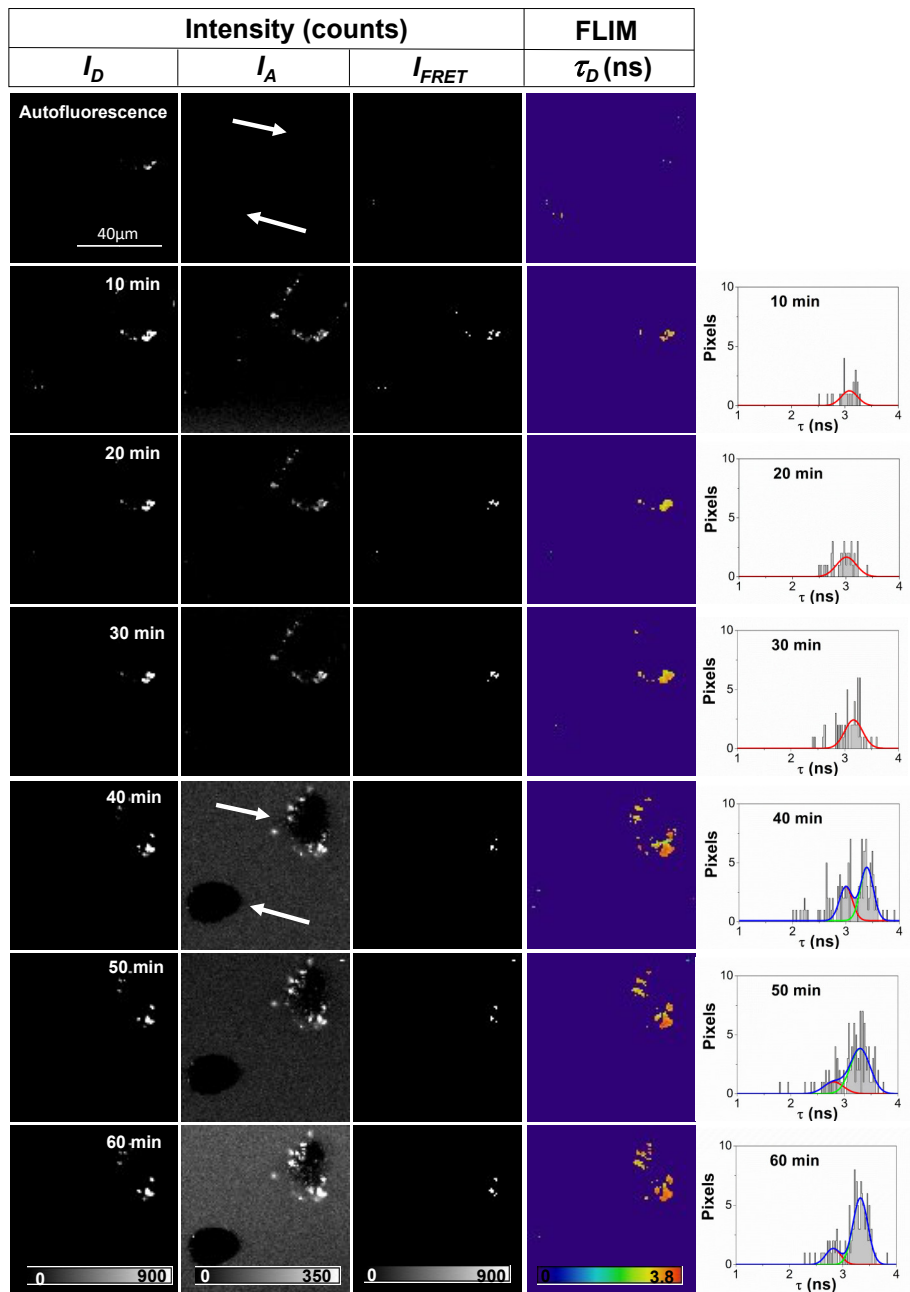
# Supplementary Material

## S1. Supplementary Figures of the Interaction of Equimolar Mixtures of Labeled A $\beta$ -488 and A $\beta$ -647 Peptides (Incubated for 15 h) with N2a Cells

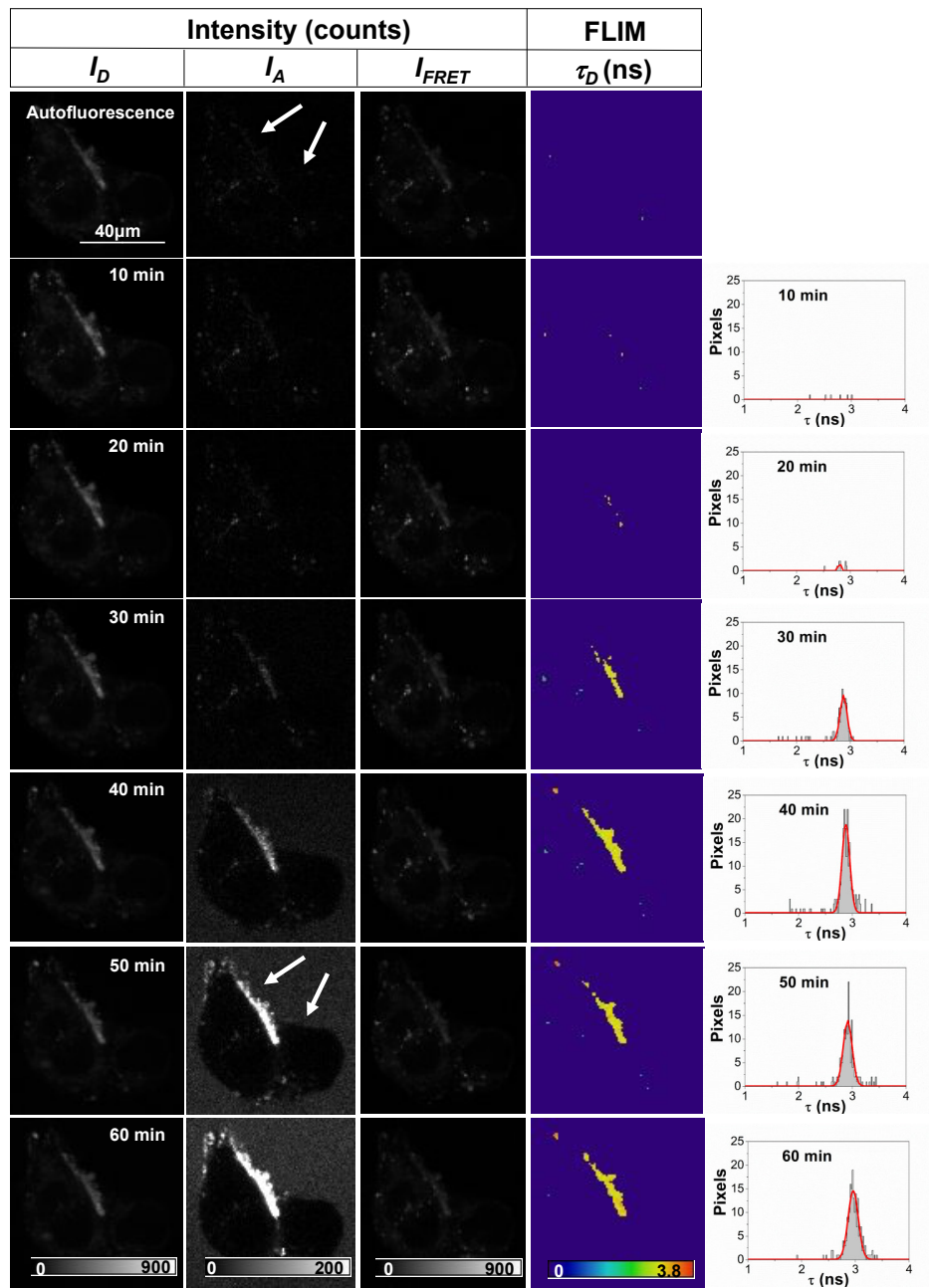
Figures S1–S4 show four representative examples of the time course of the interaction of mixed A $\beta$ -488 and A $\beta$ -647 aggregates with N2a cells. The fluorescence intensity images in the three detection windows ( $I_D$ ,  $I_{FRET}$ , and  $I_A$ ) and FLIM images of the donor fluorophore,  $\tau_D$ , are shown in parallel, with arrows indicating different detected cells for identification purposes. Histograms in the rightmost column represent  $\tau_D$  distributions for only pixels selected as aggregates. The distributions were fitted to one or two (if needed) Gaussian functions (lines).



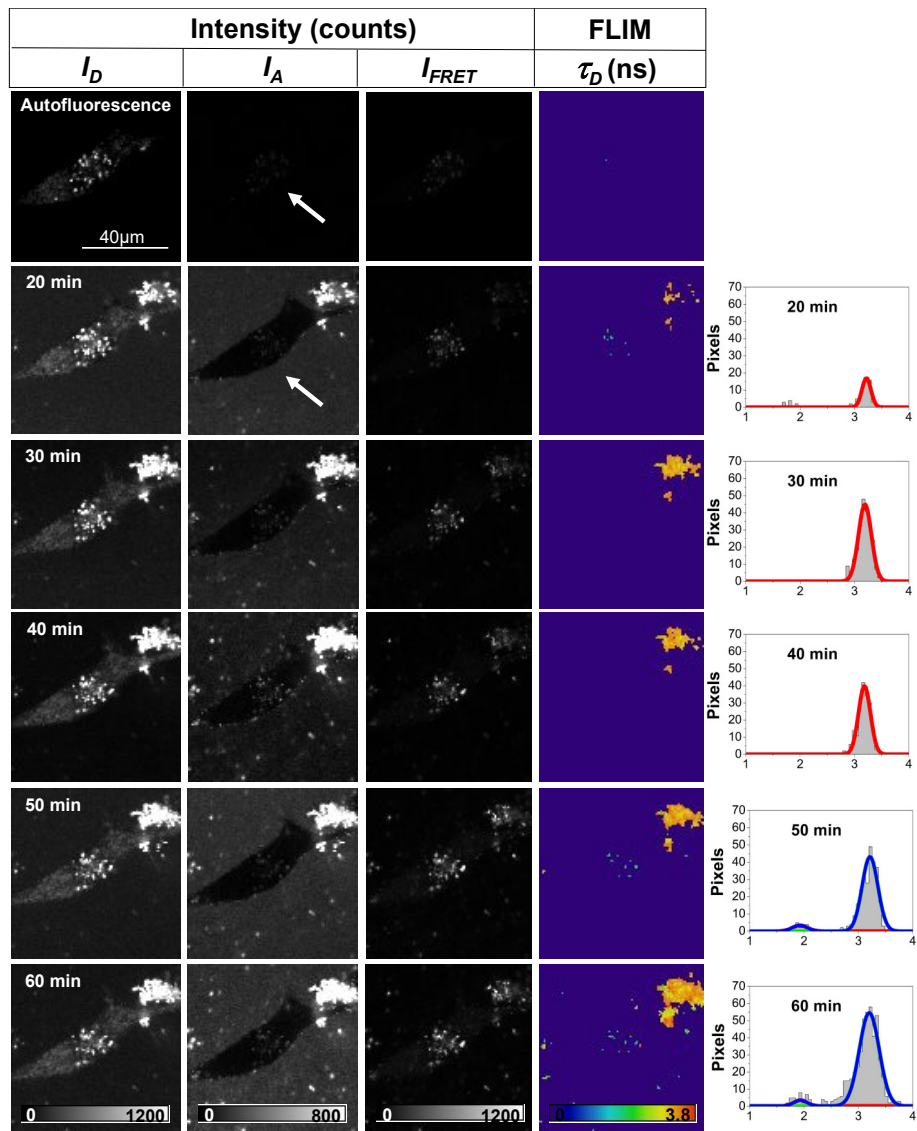
**Figure 1.** Time course of the interaction of labeled A $\beta$ 42 aggregates with N2a cells. Representative example 1.



**Figure 2.** Time course of the interaction of labeled A $\beta$ 42 aggregates with N2a cells. Representative example 2.

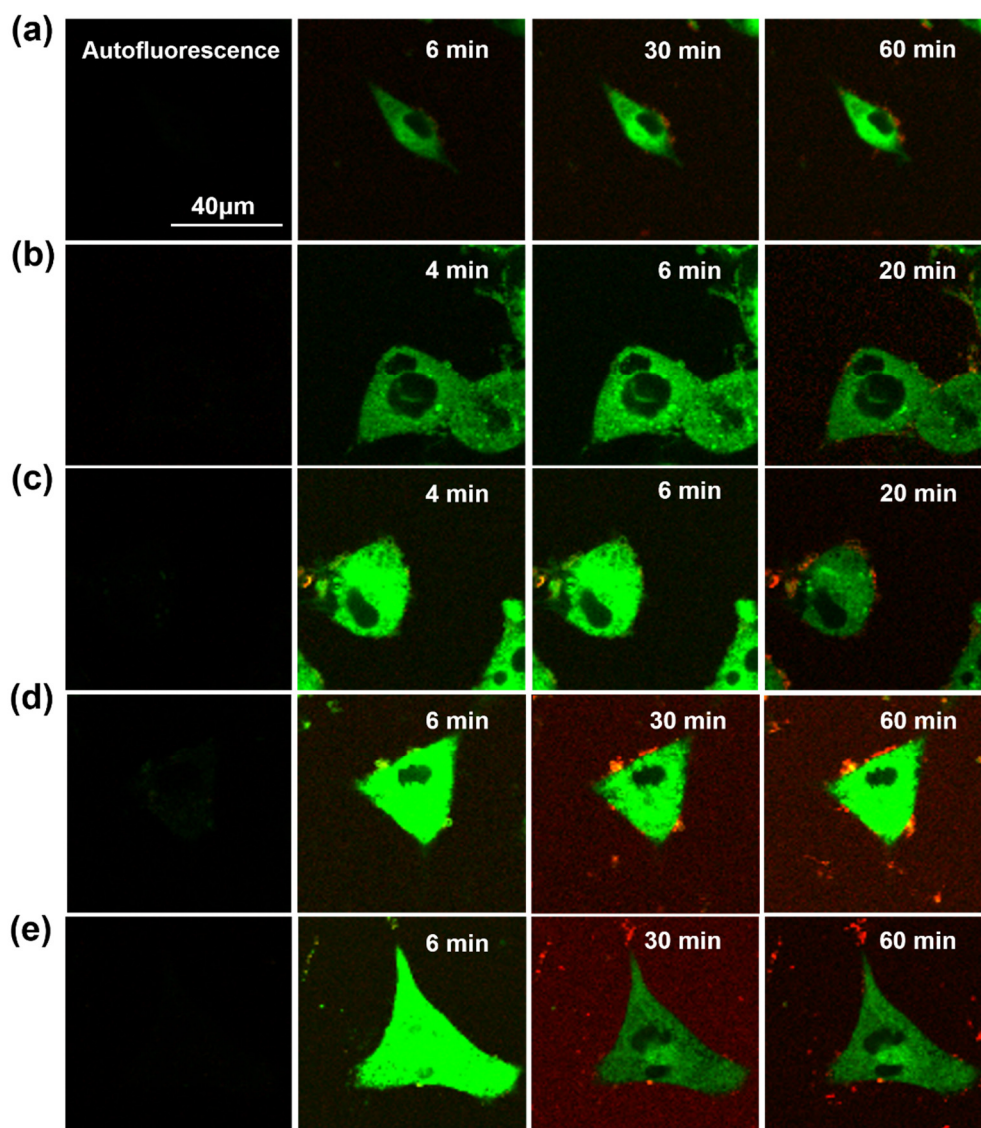


**Figure 3.** Time course of the interaction of labeled A $\beta$ 42 aggregates with N2a cells. Representative example 3.



**Figure 4.** Time course of the interaction of labeled A $\beta$ 42 aggregates with N2a cells. Representative example 4.

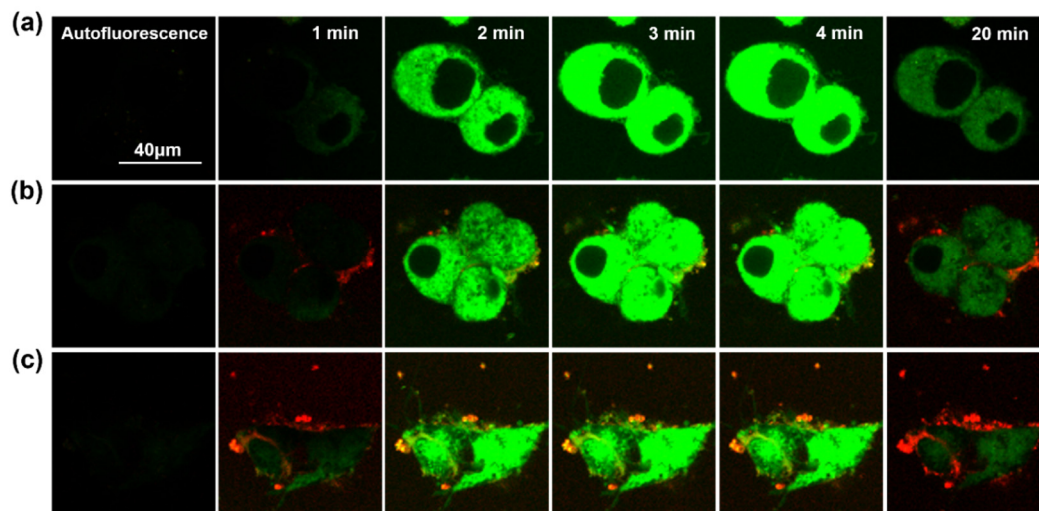
## S2. Additional Examples of Cell Stress Assays With the Biothiol Probe



**Figure 5.** Additional examples of cell stress assays with the biothiol probe (green channel), upon the addition of previously incubated A $\beta$ -647 aggregates (red channel). The images are representative examples of the effect of A $\beta$ -647 aggregates incubated for 0 (a), 1 (b), 3 (c), 24 (d) and 48 h (e).

## S3. Second Strategy for the Assay of Cellular Stress Induced by A $\beta$ -647 Aggregates

In this strategy, N2a cells and A $\beta$ -647 aggregates (red channel) interacted for 20 min prior to the addition of the biothiol fluorogenic probe (green channel), GG-DNBS. Once the fluorogenic probe is added, dual-color image collection starts. Times depicted in Figure S6 are counted from the addition of the GG-DNBS probe.



**Figure 6.** Second strategy for the assay of cellular stress induced by Aβ-647 aggregates. (a) Control experiment without added aggregates; b and c) addition of Aβ-647 aggregates incubated during 0 (b) and 1 h (c).