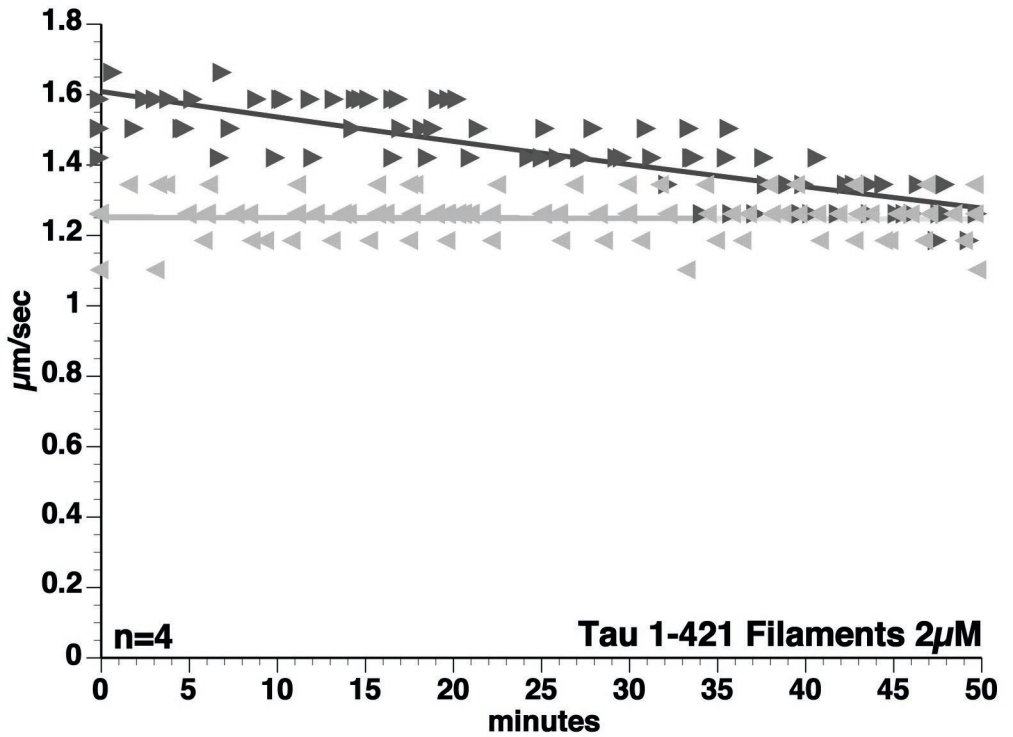
Supplemental Figure 1. The effect of 1-421 tau filaments is mediated by the activity of GSK-3. Axoplasms were perfused with filaments of 1-421 tau, and FAT rates (μm/sec) monitored over a period of 50 min. (A) Perfusion of 1-421 filaments (2 μM) specifically inhibited anterograde FAT in a time-dependent manner much as seen with filaments made from full-length tau ht40. (B) Co-perfusion of 1-421 filaments with phospho-CREB peptide (0.5 mM), a competitive inhibitor of GSK-3, blocked the effects of 1-421 filaments on FAT. These data indicate that the effects of 1-421 filaments on anterograde FAT are also mediated by activation of GSK-3. Graphs depict compiled data from at least three separate trials.

Supplemental Figure 2. Rendering of **5-ING-135** in complex with GSK-3β. This complex structure was generated from the available x-ray structure of the protein co-crystallized with staurosporine (PDB:1Q3D) with docking of the inhibitor performed using Molegro Virtual Docker program. ING-135 is a derivative of the natural product staurosporine that binds to the ATP-binding site of GSK-3, exhibiting an IC_{50} of 7nM.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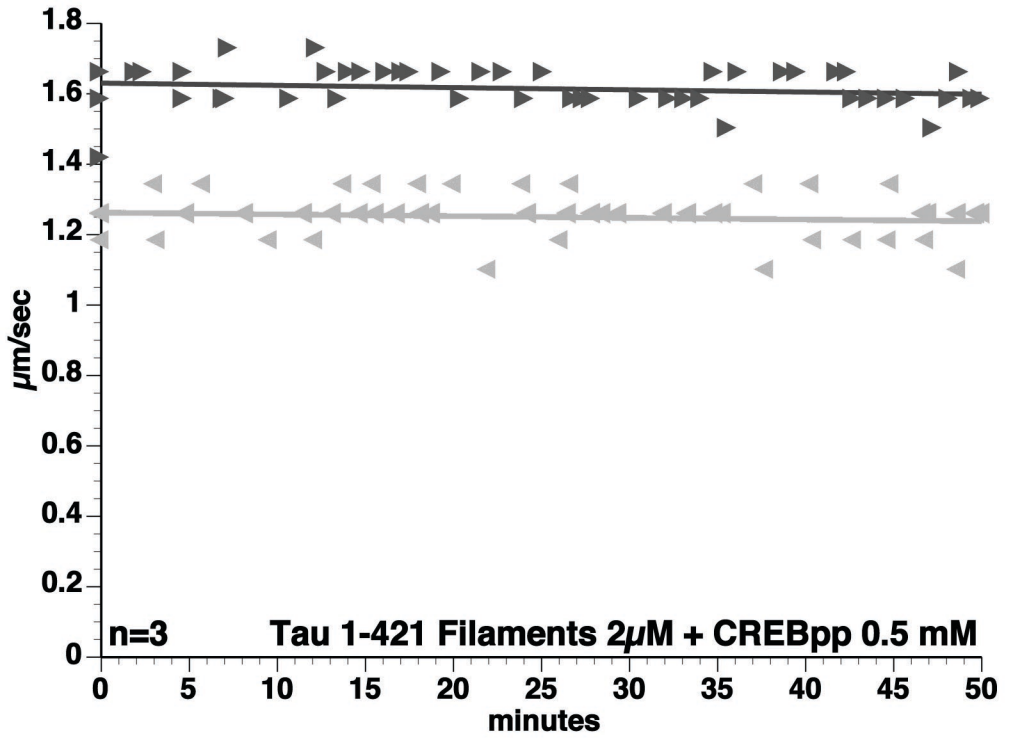
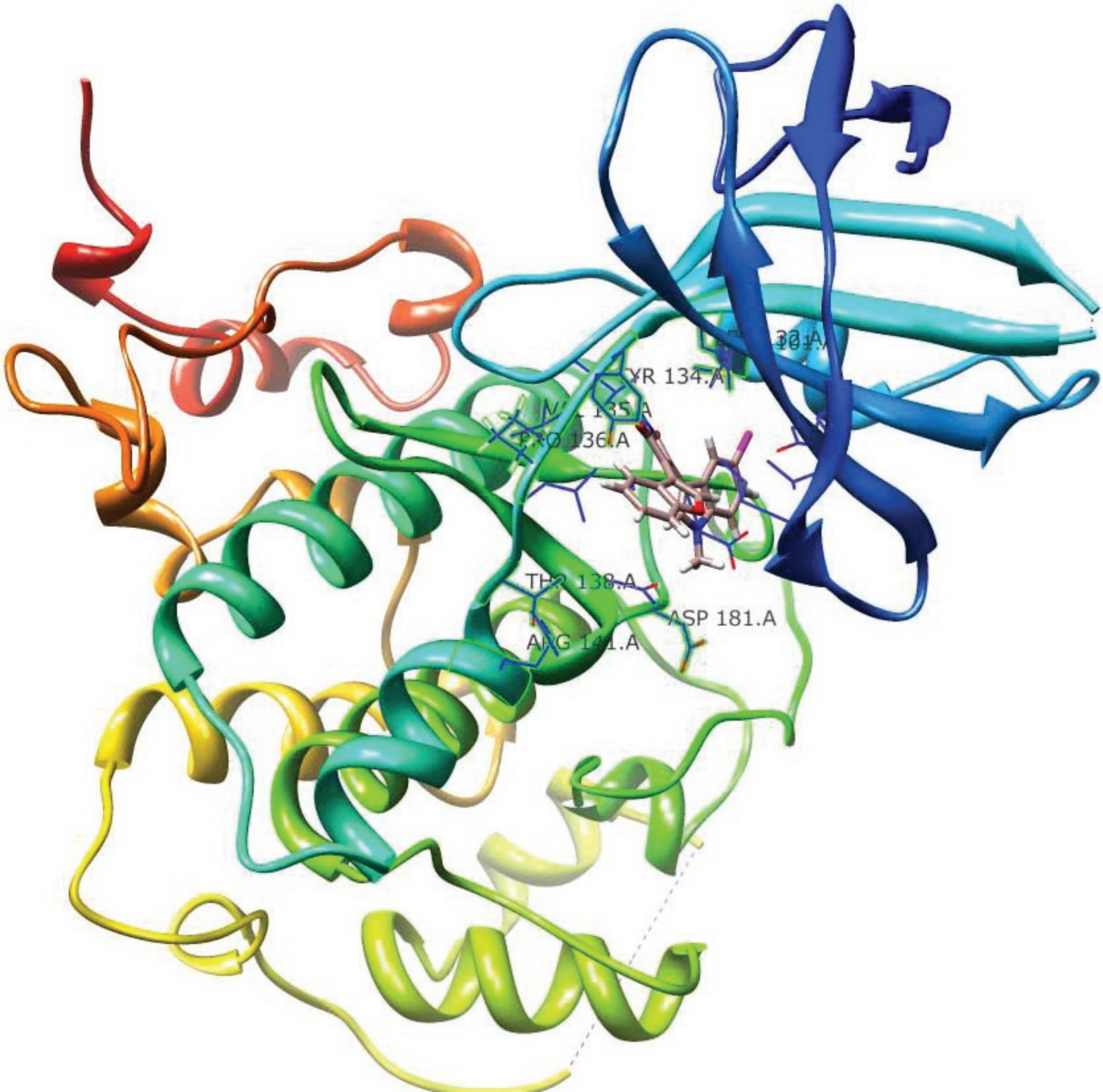
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
µm/sec
n=4
Tau 1-421 Filaments 2µM
0
5
10
15
20
25
30
35
40
45
50
minutes


1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
µm/sec
n=3
Tau 1-421 Filaments 2µM + CREBpp 0.5 mM
0
5
10
15
20
25
30
35
40
45
50
minutes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