Mechanistic insight into the disruption of Tau R3-R4 protofibril by curcumin and epinephrine: an all-atom molecular dynamics study

Yu Zou[a*], Bote Qi[a], Jingwang Tan[a], Yuxiang Sun[bc], Yehong Gong[d], Qingwen Zhang[e]

[a] Department of Sport and Exercise Science, College of Education, Zhejiang University, 886 Yuhangtang Road, Hangzhou 310058, Zhejiang, People's Republic of China. Email: zouyuzy@zju.edu.cn

[b] State Key Laboratory of Surface Physics and Department of Physics, Fudan University, 220 Handan Road, Shanghai 200433, People's Republic of China

[c] Department of Physics, Ningbo University, 818 Fenghua Road, Ningbo 315211, Zhejiang, People's Republic of China

[d] School of Sports Science and Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, People's Republic of China

[e] College of Physical Education and Training, Shanghai University of Sport, 399 Changhai Road, Shanghai 200438, People's Republic of China

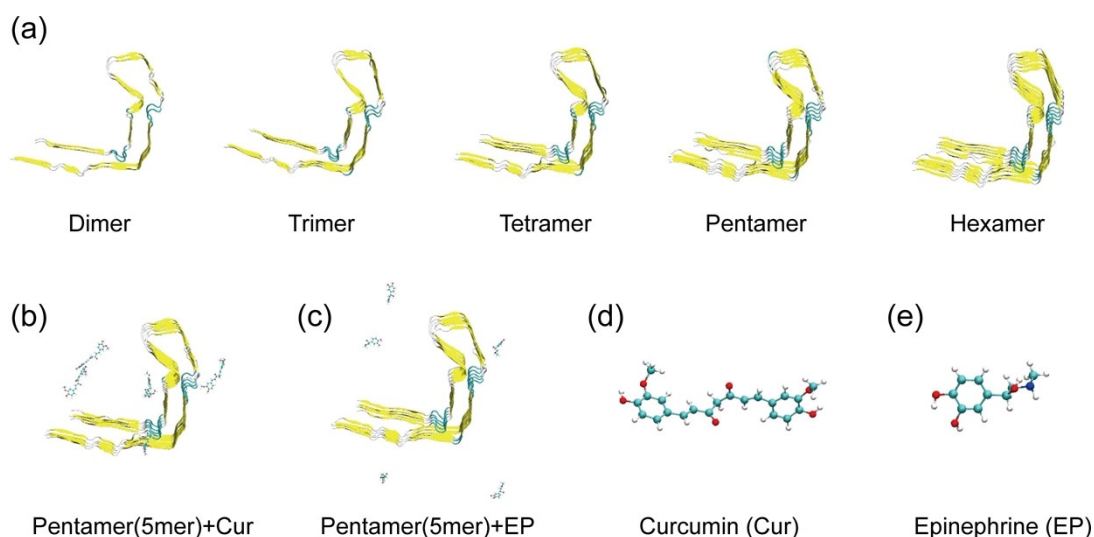**This material contains seven supplemental figures.**

Fig. S1 Initial states of each Tau oligomer (a), 5mer+Cur system (b) and 5mer+EP system (c), and the chemical structures of Cur (d) and EP (e).
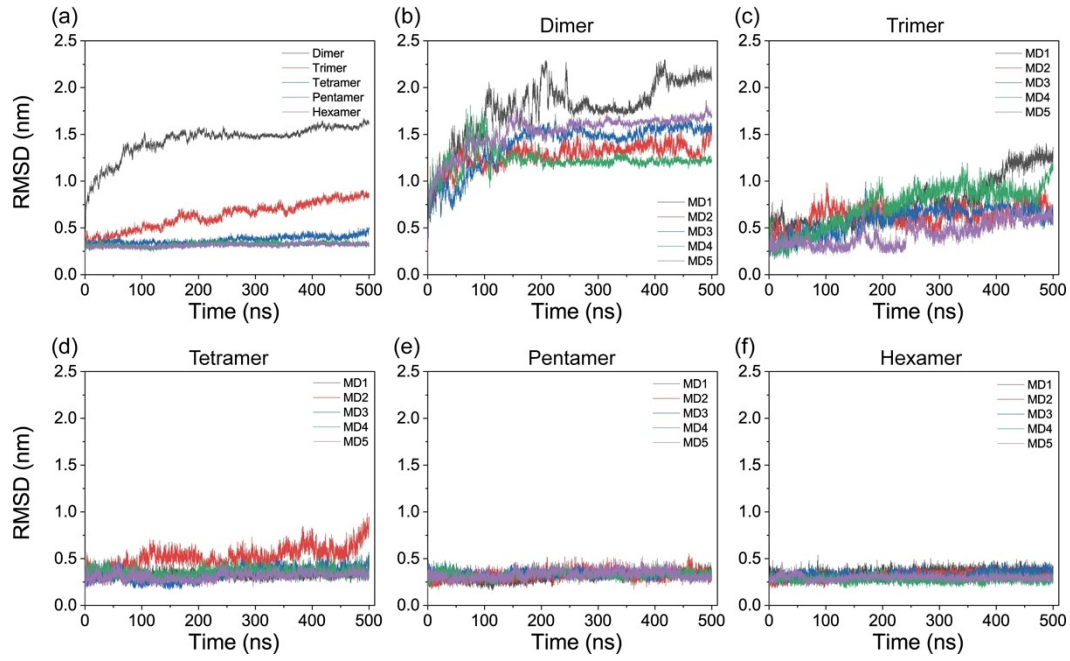
Fig. S2 Time evolution of average RMSD values of Tau oligomers over five MD runs for each system (a). RMSD values of different sizes of Tau oligomers (b-f) as a function of simulation time.
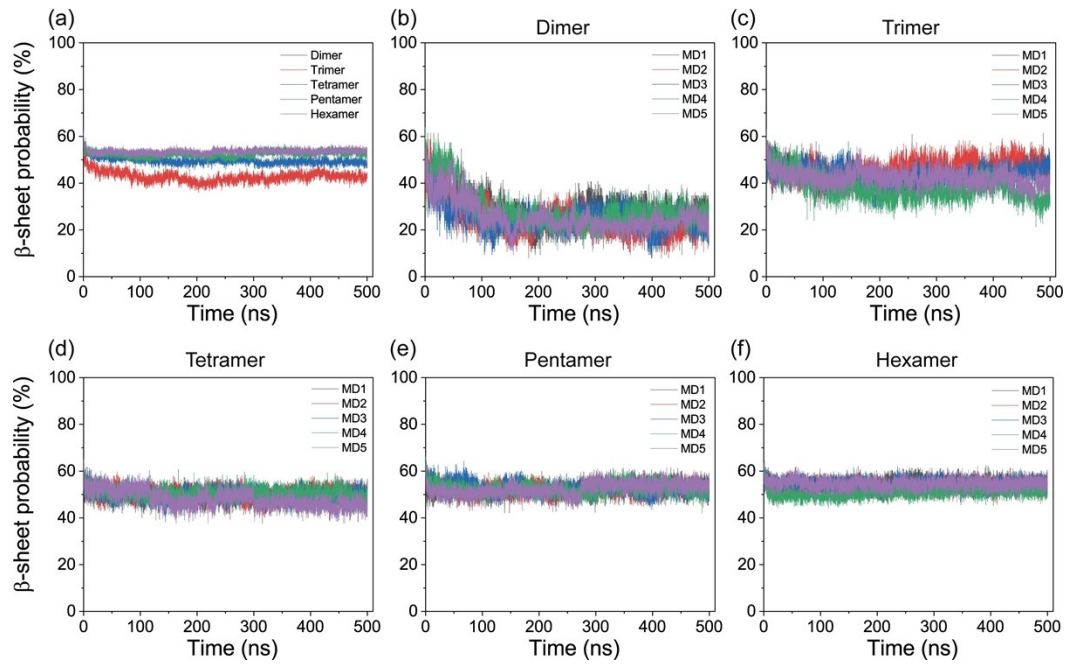

Fig. S3 Time evolution of average β-sheet probabilities of Tau oligomers over five MD runs for each system (a). β-sheet probabilities of different sizes of Tau oligomers (b-f) as a function of simulation time.

Fig. S4 PDF of the distance between the positively charged group of the side chain and two rings of Cur (a, b).

Fig. S5 The residue-based contact number and fraction of reduced β-sheet in 5mer+Cur (a) and 5mer+EP (b) systems. The probabilities of reduced β-sheet were calculated using the residue-based β-sheet probabilities of Tau pentamer in 5mer system minus those in 5mer+Cur and 5mer+EP systems.

5mer+Cur

MD1 MD2 MD3 MD4 MD5

R379

S305

Cluster-1 Cluster-1 Cluster-1 Cluster-1 Cluster-1
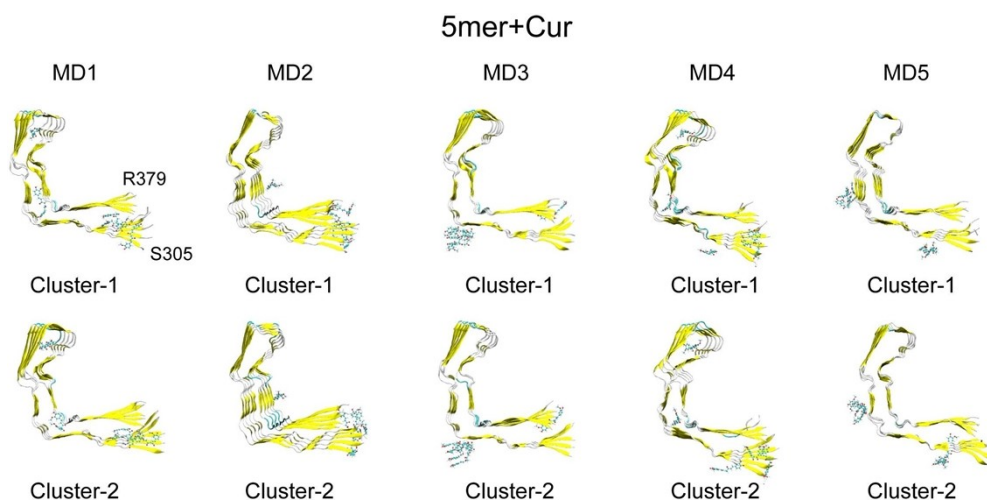
Cluster-2 Cluster-2 Cluster-2 Cluster-2 Cluster-2

Fig. S6 Representative conformations of the first two most-populated clusters of Tau pentamer in

5mer+Cur system in five MD runs.

5mer+EP

MD1 MD2 MD3 MD4 MD5

R379

S305

Cluster-1 Cluster-1 Cluster-1 Cluster-1 Cluster-1

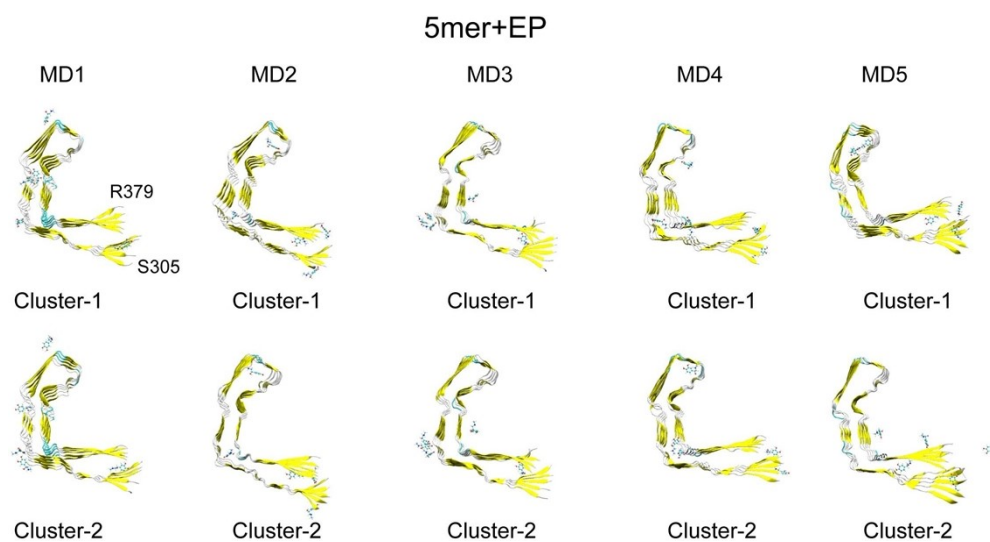Cluster-2 Cluster-2 Cluster-2 Cluster-2 Cluster-2

Fig. S7 Representative conformations of the first two most-populated clusters of Tau pentamer in

5mer+EP system in five MD runs.