Supporting Information

Cationic polymethacrylate-copolymer acts as an agonist for β-amyloid and antagonist for amylin fibrillation

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List of acronyms and abbreviations:

β-amyloid	Beta-amyloid
AD	Alzheimer's disease
CD	Circular dichroism
FT-IR	Fourier-transform infrared spectroscopy
HMQC	Heteronuclear Multiple-Quantum Correlation
MD	Molecular dynamics
MM/PBSA	Molecular mechanics Poisson-Boltzmann surface area
NMR	Nuclear Magnetic Resonance
PMA	Polymethacrylate
QA	Quaternary ammonium
RMSD	Root mean square deviation
RMSF	Root mean square fluctuation
SOFAST	Selective optimized flip angle short transient
T2D	Type-2 Diabetes
ThT	Thioflavin-T

Table S1. Interaction map of β-amyloid-1-40 and PMAQA derived from 1 μs all-atom MD simulation.

PMAQA binding β-amyloid-1-40 residues	Interaction type
GLU22:OE1	Electrostatic
ASP23:OD1	Electrostatic
GLU22:OE1	Electrostatic
SER26:HG	Hydrogen Bond
ASN27:O	Hydrogen Bond
SER26:O	Hydrogen Bond
ASN27:O	Hydrogen Bond
GLU22:OE2	Hydrogen Bond
GLU22:OE1	Hydrogen Bond
ASP23:OD1	Hydrogen Bond
ASP23:OD1	Hydrogen Bond
ASP23:OD2	Hydrogen Bond
GLU22:OE1	Hydrogen Bond
LEU17:O	Hydrogen Bond
LEU17:O	Hydrogen Bond
VAL24	Hydrophobic
ILE31	Hydrophobic
ILE32	Hydrophobic
PHE20	Hydrophobic

Table S2. Interaction map of amylin and PMAQA derived from 0.7 μs all-atom MD simulation.

PMAQA binding amylin residues	Interaction type
ILE26:H	Hydrogen Bond
SER34:HG	Hydrogen Bond
TYR37:HH	Hydrogen Bond
SER34:O	Hydrogen Bond
ASN21:O	Hydrogen Bond
ASN31:OD1	Hydrogen Bond
ILE26:O	Hydrogen Bond
SER28:O	Hydrogen Bond
SER28:O	Hydrogen Bond
THR30:O	Hydrogen Bond
TYR37	Hydrphobic
TYR37	Hydrphobic
TYR37	Hydrphobic

β–amyloid-1-40: ^{1}DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV^{40}

Amylin: ^{1}KCNTATCATQRLANFLVHSSNNFGAILSSTNVGSNTY-NH_2^{37}

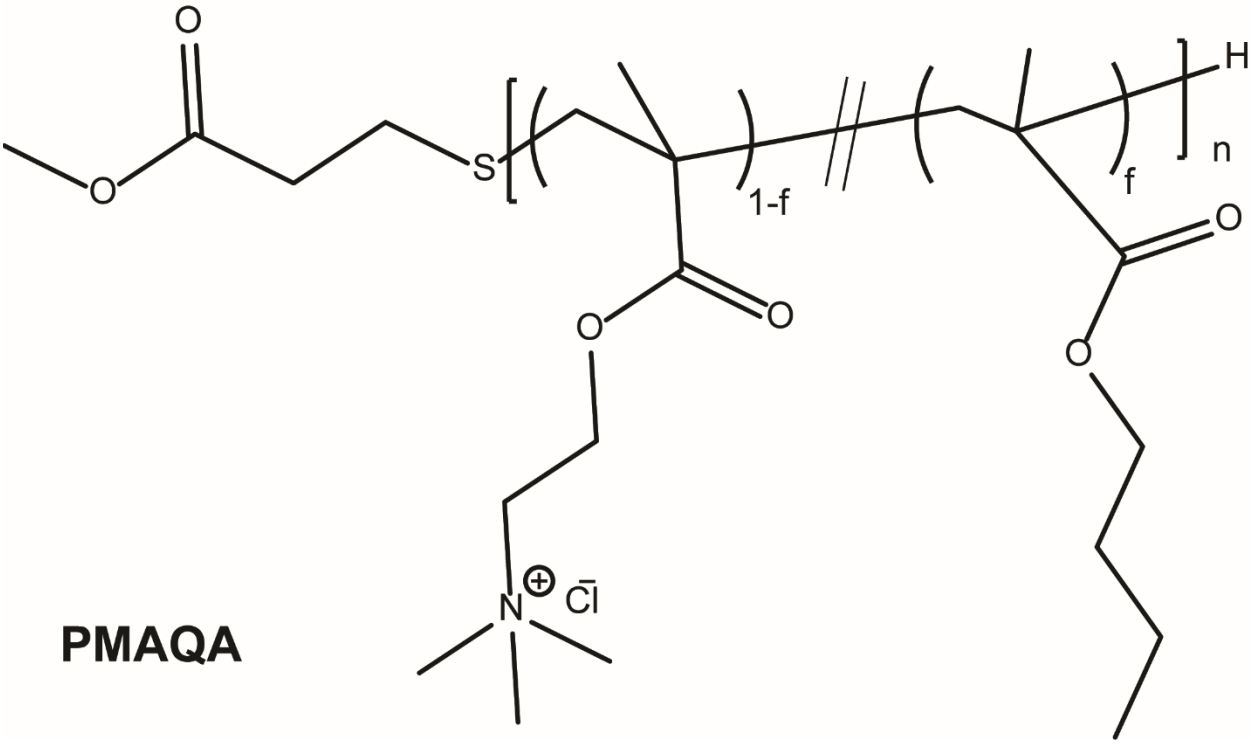

Figure S1. Amino acid sequences of a 40-residue β-amyloid-1-40 and 37-residue amylin (top). 2D structure of the PMAQA polymer used in this study. "f" denotes the fraction of hydrophobic unit.

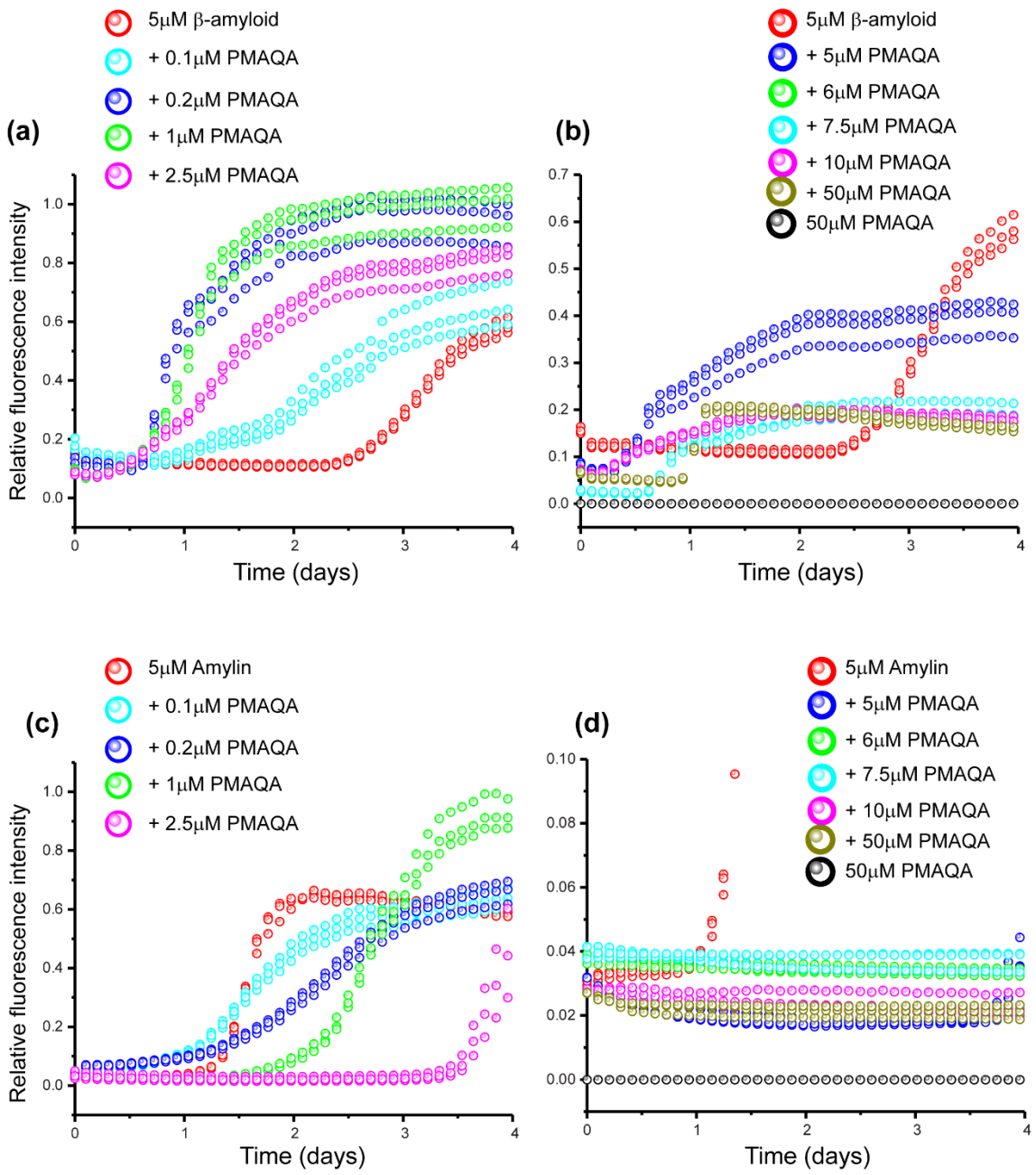

Figure S2. Aggregation kinetics of β-amyloid-1-40 and amylin. (a) ThT fluorescence shows aggregation kinetics of 5 μM β-amyloid-1-40 dissolved in 10 mM sodium phosphate buffer, pH 7.4 at variable substoichiometric (a) and superstoichiometric (b) PMAQA concentration in triplicate. The aggregation kinetics of 5 μM amylin dissolved in 30 mM sodium acetate buffer, pH 5.5 at variable substoichiometric (c) and superstoichiometric (d) PMAQA concentration in triplicate.

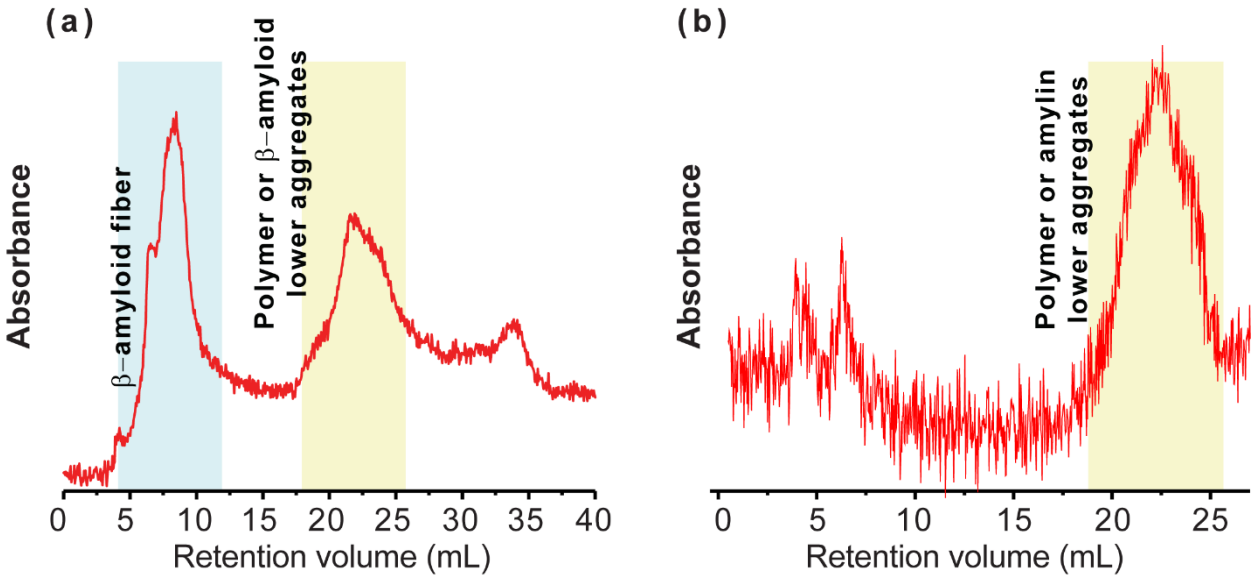

Figure S3. Size-exclusion chromatography profiles of (a) 10 μM β-amyloid-1-40 incubated with 15 μM PMAQA for 5 minutes at room temperature prior to SEC run, (b) 10 μM amylin incubated with 15 μM PMAQA for overnight at room temperature with gentle shaking prior to SEC run.

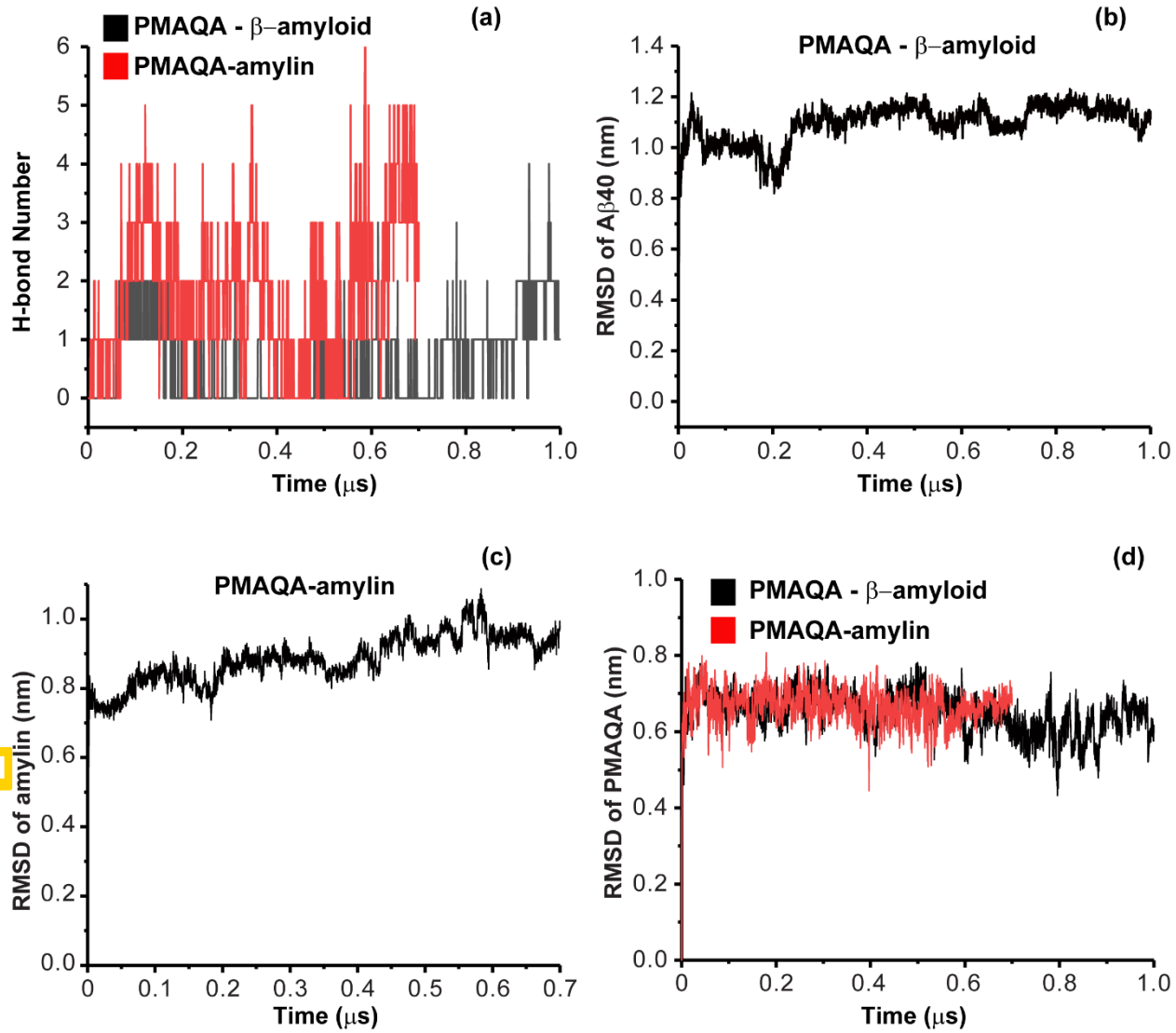

Figure S4. MD analysis of PMAQA binding to β-amyloid-1-40 or amylin. (a) Intermolecular hydrogen bond formation between PMAQA and β-amyloid-1-40 or amylin with respect to simulation time at the indicated colors. The stability parameter derived from the protein backbone atoms in β-amyloid-1-40 (b) or amylin (c) and all-atoms in PMAQA (d) is interpreted using their average root mean square deviation (RMSD) as a function of time.

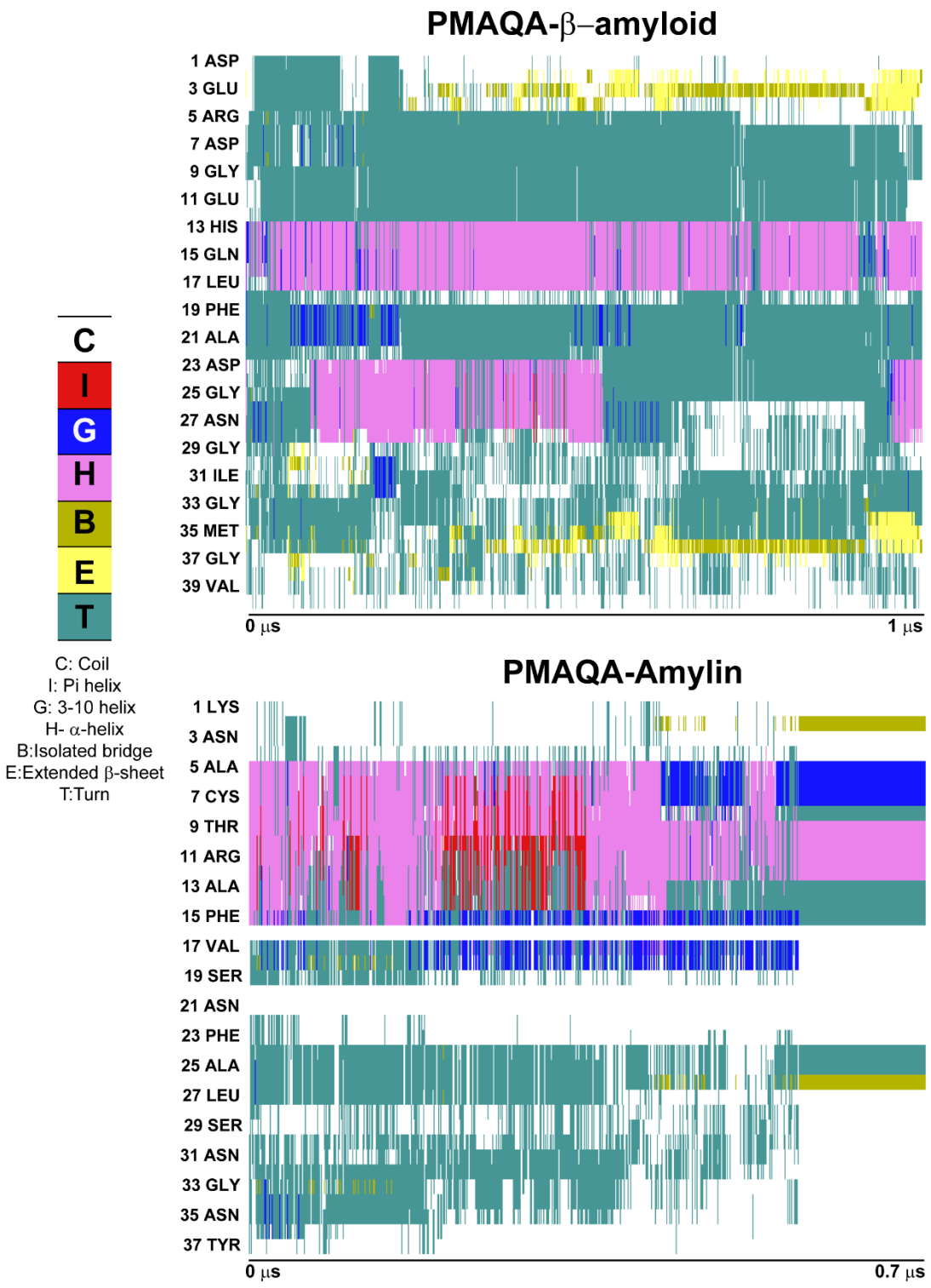

Figure S5. Secondary structural changes in β-amyloid-1-40 (top) or amylin (bottom) as a function of simulation time. The images are generated using VMD and the legends of secondary structural unit are shown in the left.

Movie S1. HS-AFM observation of seeding reaction of 5μM amylin in APTES-mica.

Movie S2. HS-AFM observation of seeding reaction of 5μM amylin in presence of equimolar PMAQA in APTES-mica.