Electronic Supplementary Material (ESI) for RSC Advances.

SUPPORTING INFORMATION

Ameliorating Amyloid Aggregation through Osmolytes as a Probable Therapeutic Molecule against Alzheimer's disease and Type 2 Diabetes

Anchala Kumari

1. Department of Biotechnology, Teri School of Advanced Studies, New Delhi-110070, India
2. School of Biotechnology, Jawaharlal Nehru University, New Delhi-110067, India

Email: anchala.choudhary27@gmail.com

Pallavi Somvanshi

Department of Biotechnology, Teri School of Advanced Studies, New Delhi-110070, India
Email: psomvanshi@gmail.com

Abhinav Grover

School of Biotechnology, Jawaharlal Nehru University, New Delhi-110067, India
Email: abhinavgr@gmail.com

Corresponding Author

Dr. Pallavi Somvanshi
Associate Professor
Department of Biotechnology, Teri School of Advanced Studies, New Delhi-110070, India
Tel No.: +91-9899931682
Email address: psomvanshi@gmail.com

Dr. Abhinav Grover
Assistant Professor
School of Biotechnology, Jawaharlal Nehru University, New Delhi, India
Tel No.: +91-8130738032
Fax: +91-11-26702040
Email address: abhinavgr@gmail.com

Supplementary Figure Legends

Figure S1 - Convergence check for REMD run of A-Beta and hIAPP showing (*A*) replica index and (*B*) replica temperature exchange plot along the simulation time for all the six systems (*C*) Distribution of potential energy of each replica along the simulation time.

Figure S2 - Population density analysis for A-Beta and hIAPP, peptide end to end distance (R_{ee}) i.e. C to N terminal and radius of gyration (R_g) around its center of mass at four different time windows [0-25, 25-50, 50-75 and 75-100 ns]. Blue part implies the heavily populated conformations, whereas red and yellow part indicates the limited populated conformations.

Figure S3 - Probability percentage (%) of intramolecular hydrogen bonds (C=O to N=H) formation of A-Beta and hIAPP peptides at four different time windows [0-25, 25-50, 50-75 and 75-100 ns].

Figure S4 - Population density analysis of monomeric salt bridges within ASP (D) and LYS (K) of A-Beta at four different time windows [0-25, 25-50, 50-75 and 75-100 ns].

Figure S5 - Secondary structure analysis showing detailed residue specific probability % of B-Bridge, Bend, Turn, 3-Helix and 5-Helix for A-Beta and hIAPP.

Figure S6 - (*A*) Secondary structure probability percentage (%) of A-Beta and hIAPP peptides at four time frames [0-25, 25-50, 50-75 and 75-100 ns]. (*B-E*) Residue wise secondary structure probability percentage (%) of A-Beta and hIAPP peptides at four time frames [(*B*) 0-25 ns; (*C*) 25-50 ns; (*D*) 50-75 ns and (*E*) 75-100 ns]

Figure S7 - Ideal conformations of highest populated clusters of A-Beta and hIAPP raised in different conditions at four different time windows [0-25, 25-50, 50-75 and 75-100 ns].

Figure S8 - A-Beta and hIAPP monomer conformation in existence of G-HCL and L-PRO in structural resolution of 0.5 nm from the A-Beta and hIAPP surface. A-Beta and hIAPP displayed as cartoon representation (rainbow) and osmolytes displayed as spheres and dots representation (heteroatoms color: G-HCL: blue, red and grey and L-PRO: green, red and grey).

Figure S9 - Distribution of osmolytes at varied distances around each residues of the A-Beta and hIAPP backbone for most dominant conformation at four different time frames [0-25, 25-50, 50-75 and 75-100 ns]. G-HCL tends to densely accumulate around positively charged side chain residues while L-PRO lacks this property.

Figure S10 - Radial distribution function**,** g(r), of water and osmolytes (G-HCL and L-PRO) with respect to the (*A*) A-Beta and (*B*) hIAPP peptide surface at four different time frames [0-25, 25-50, 50-75 and 75-100 ns].

Supplementary Figures

Figure S1

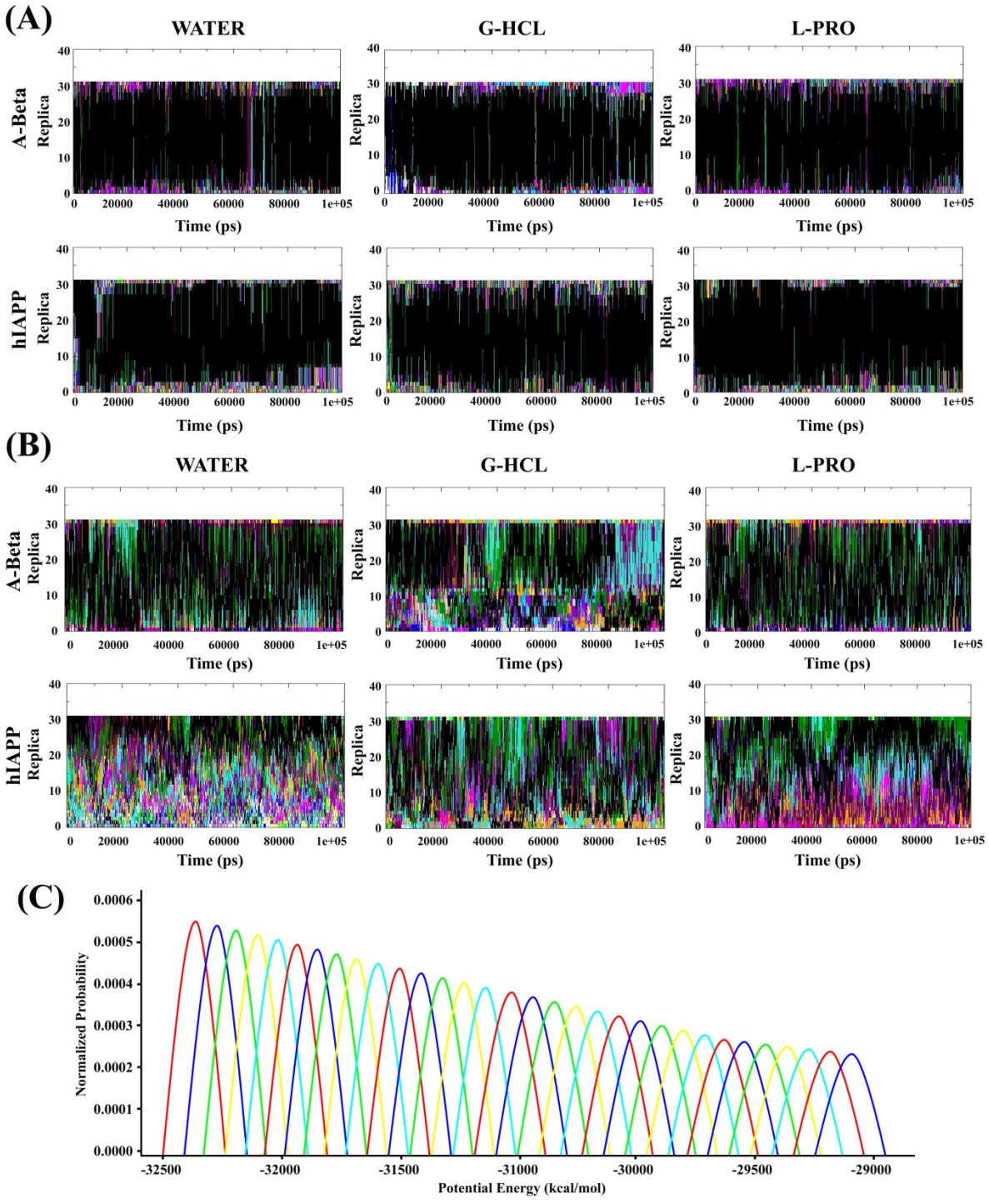


Figure S2

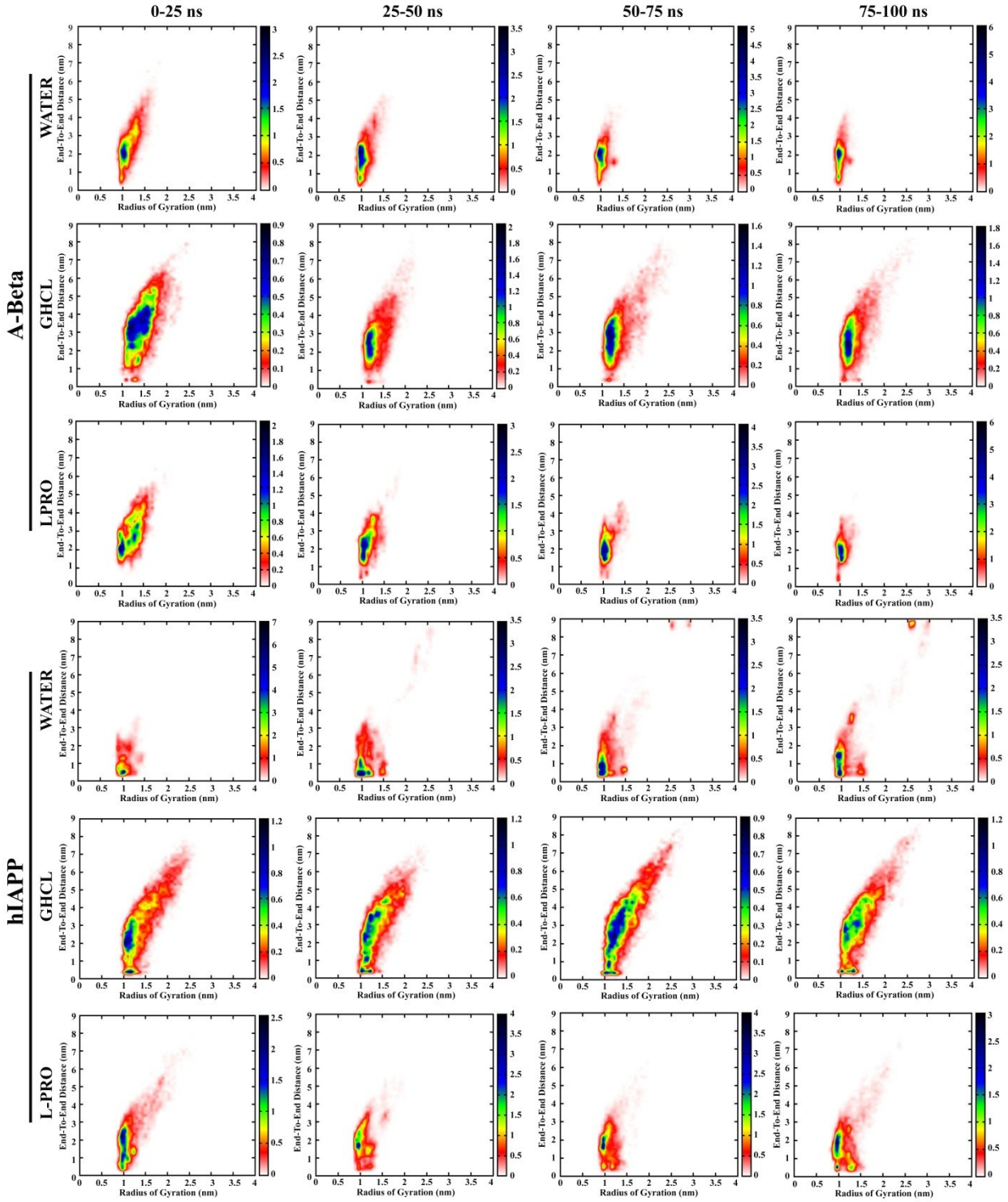

0-25 ns
25-50 ns
50-75 ns
75-100 ns
A-Beta
hIAPP
WATER
GHCL
LPRO
L-PRO
End-To-End Distance (nm)
Radius of Gyration (nm)

Figure S3

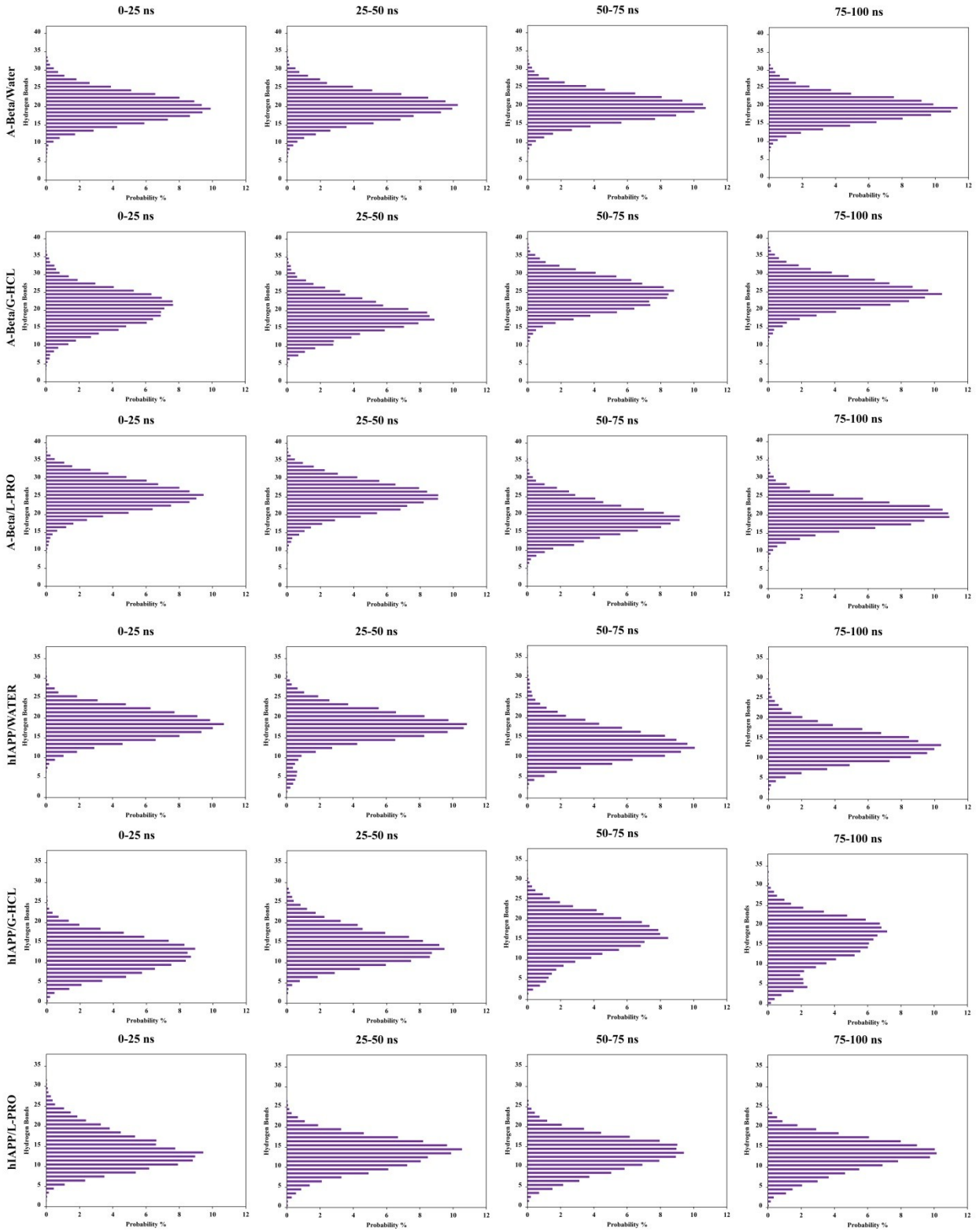

0-25 ns
25-50 ns
50-75 ns
75-100 ns
A-Beta/Water
A-Beta/G-HCL
A-Beta/L-PRO
hIAPP/WATER
hIAPP/G-HCL
hIAPP/L-PRO
Hydrogen Bonds
Probability %

Figure S4

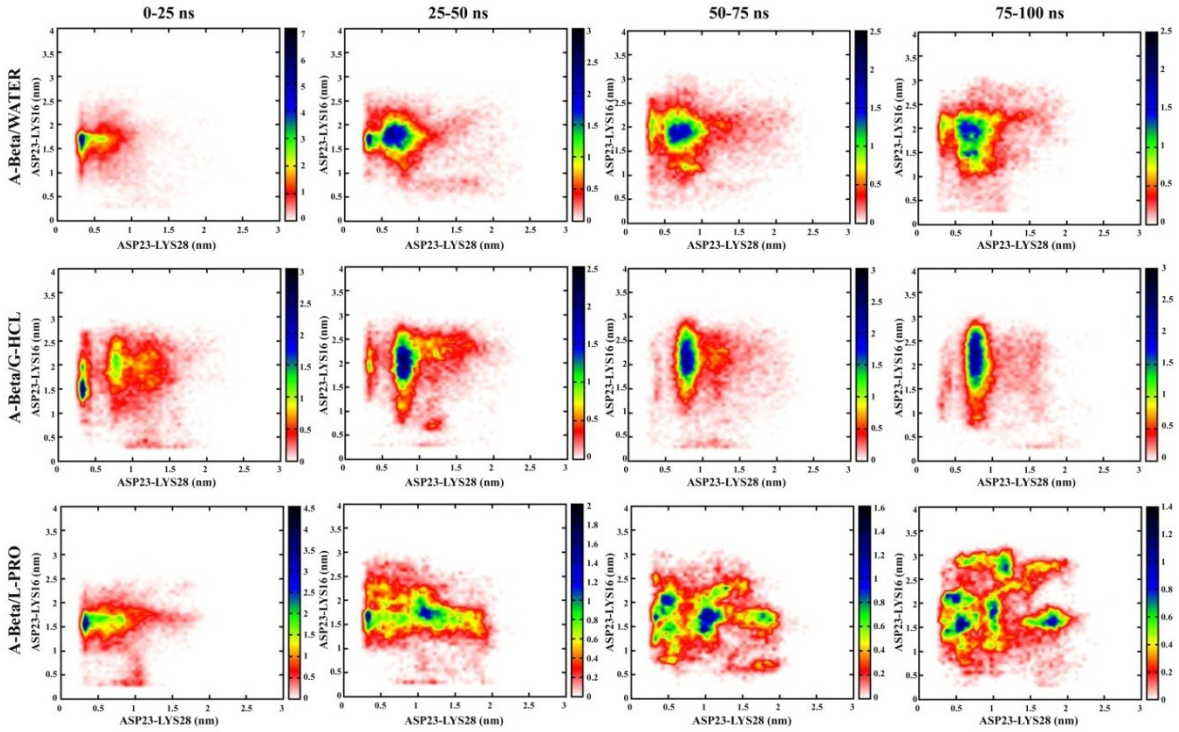

0-25 ns
25-50 ns
50-75 ns
75-100 ns
A-Beta/WATER
A-Beta/G-HCL
A-Beta/L-PRO
ASP23-LYS16 (nm)
ASP23-LYS28 (nm)

Figure S5

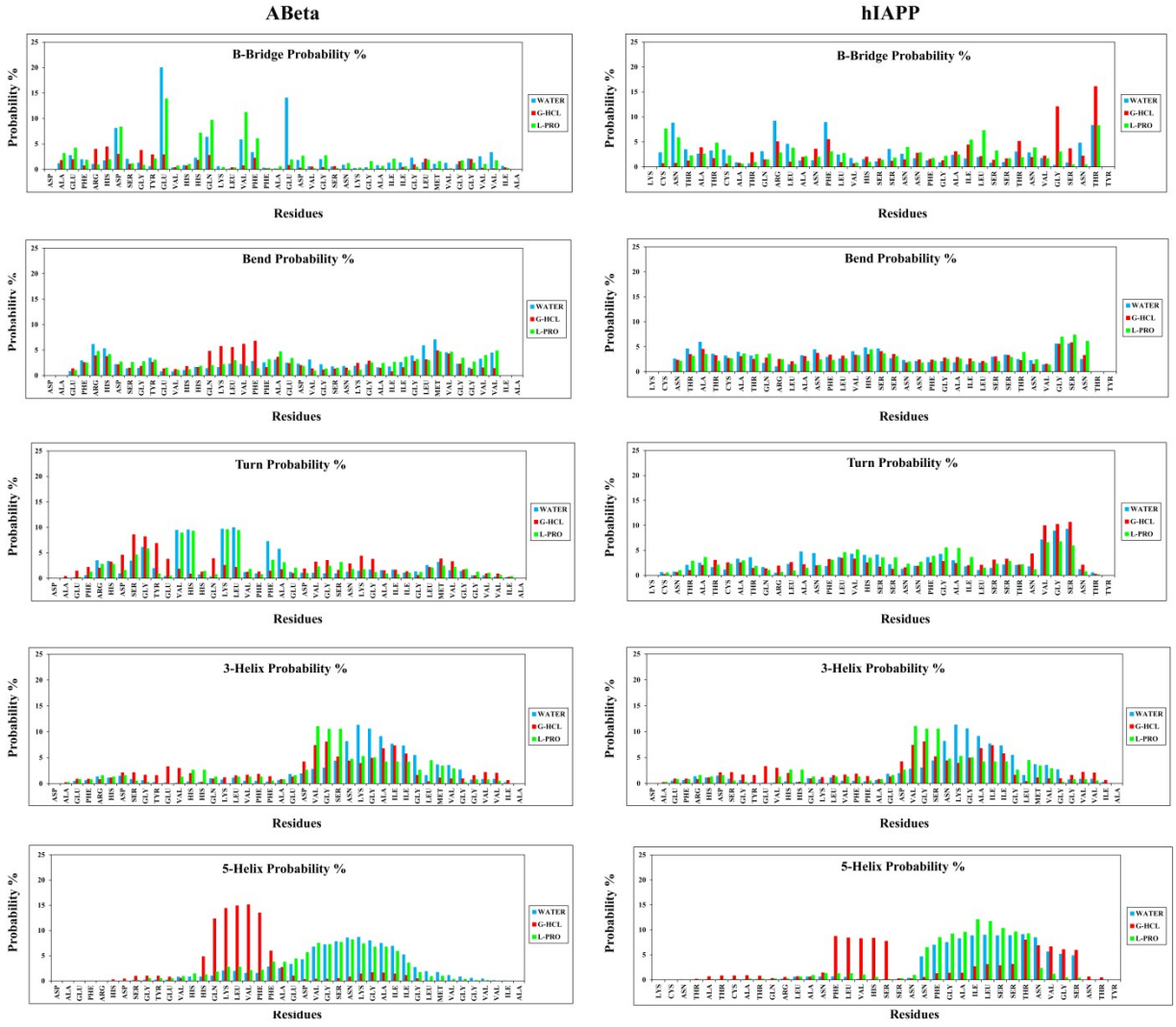

ABeta
hIAPP
B-Bridge Probability %
Bend Probability %
Turn Probability %
3-Helix Probability %
5-Helix Probability %
Probability %
Residues
WATER
G-HCL
L-PRO

Figure S6*A*

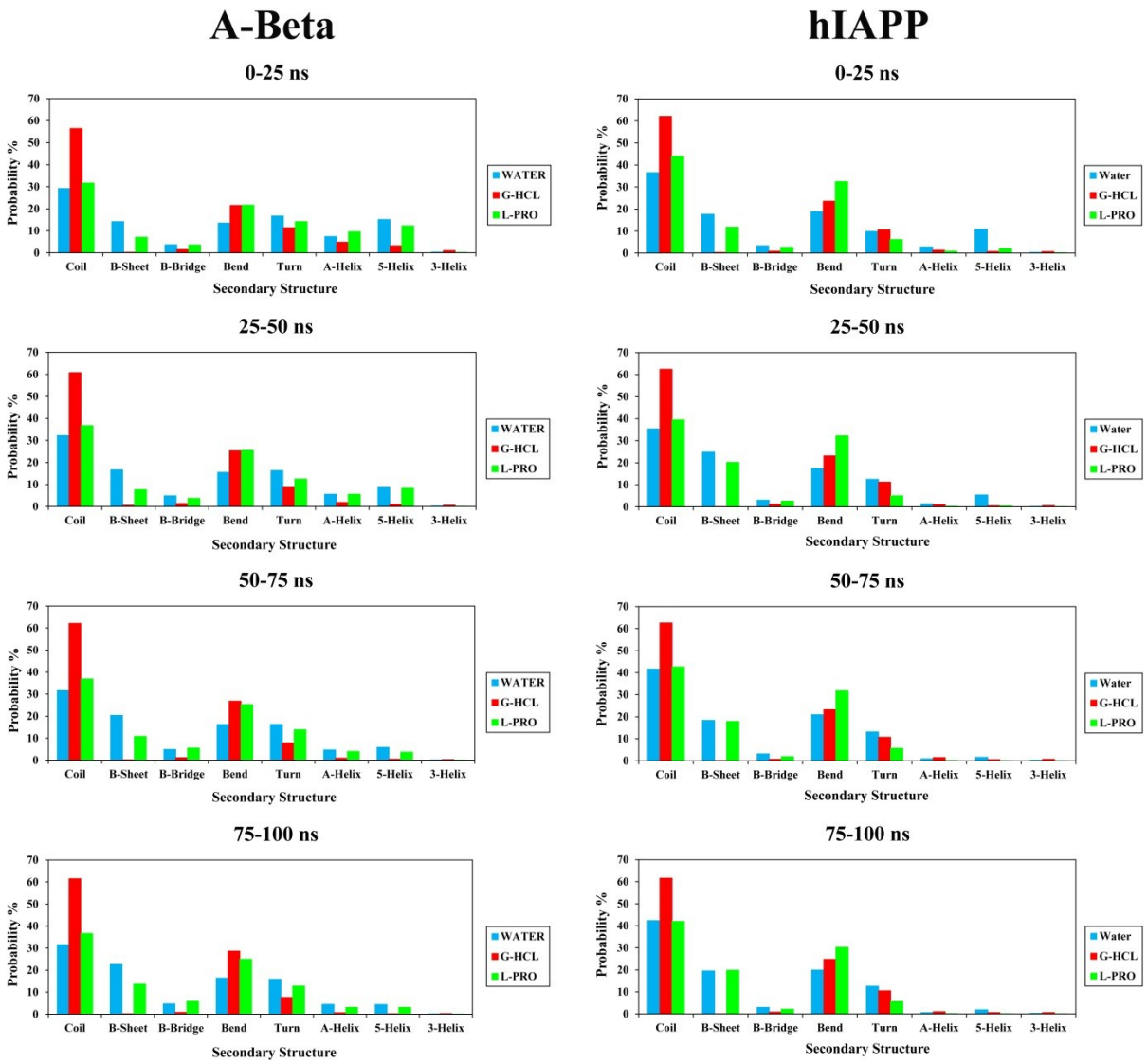

A-Beta
hIAPP
0-25 ns
25-50 ns
50-75 ns
75-100 ns
Probability %
Secondary Structure
Coil
B-Sheet
B-Bridge
Bend
Turn
A-Helix
5-Helix
3-Helix
WATER
G-HCL
L-PRO
Water

Figure S6*B*

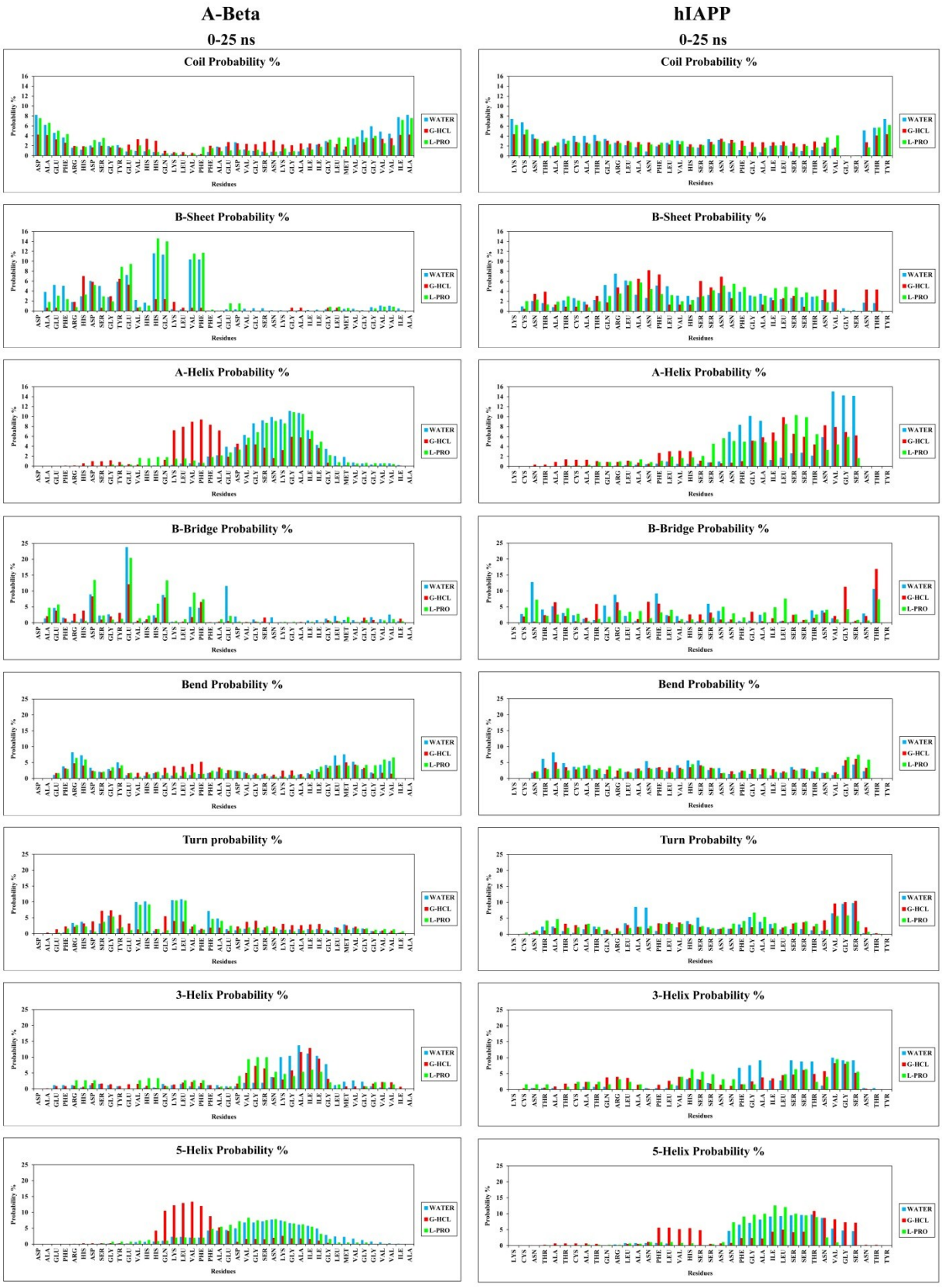

A-Beta
0-25 ns
hIAPP
0-25 ns
Coil Probability %
B-Sheet Probability %
A-Helix Probability %
B-Bridge Probability %
Bend Probability %
Turn probability %
Turn Probabilty %
3-Helix Probability %
5-Helix Probability %
Probability %
Residues
WATER
G-HCL
L-PRO

Figure S6*C*

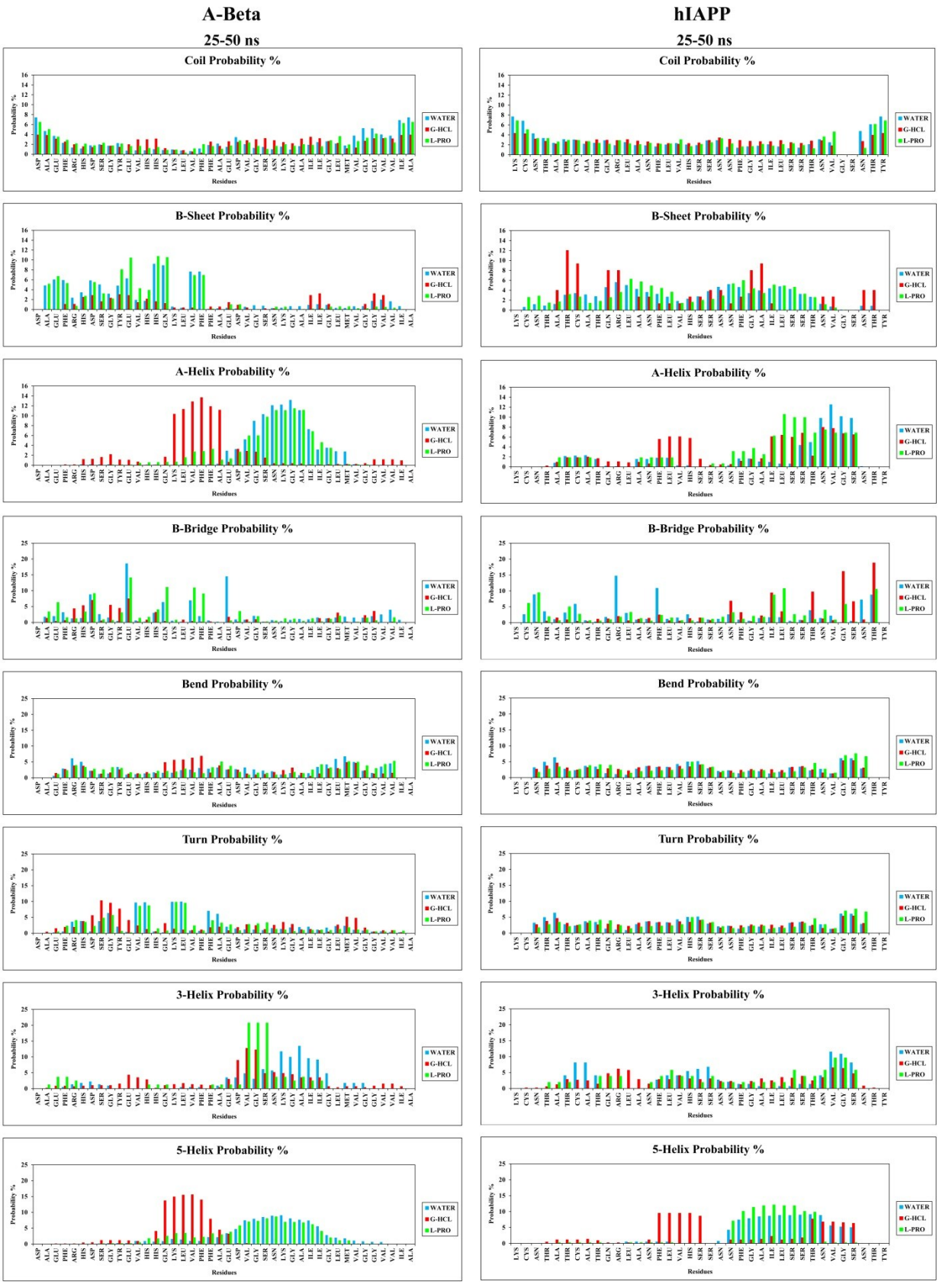

A-Beta
25-50 ns
hIAPP
25-50 ns
Coil Probability %
B-Sheet Probability %
A-Helix Probability %
B-Bridge Probability %
Bend Probability %
Turn Probability %
3-Helix Probability %
5-Helix Probability %
Probability %
Residues
WATER
G-HCL
L-PRO

Figure S6*D*

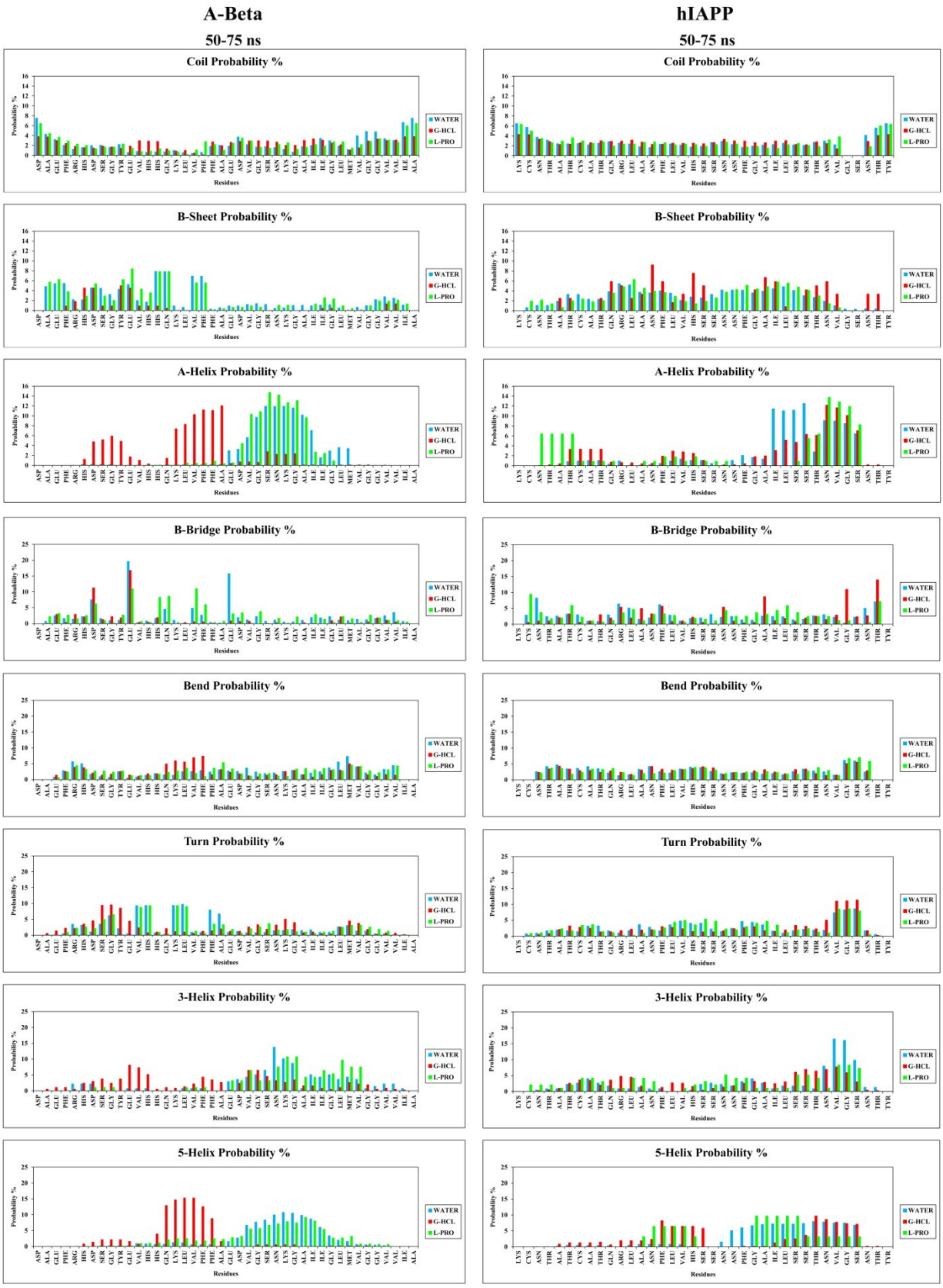

A-Beta
50-75 ns
hIAPP
50-75 ns
Coil Probability %
B-Sheet Probability %
A-Helix Probability %
B-Bridge Probability %
Bend Probability %
Turn Probability %
3-Helix Probability %
5-Helix Probability %
Probability %
Residues
WATER
G-HCL
L-PRO

Figure S6*E*

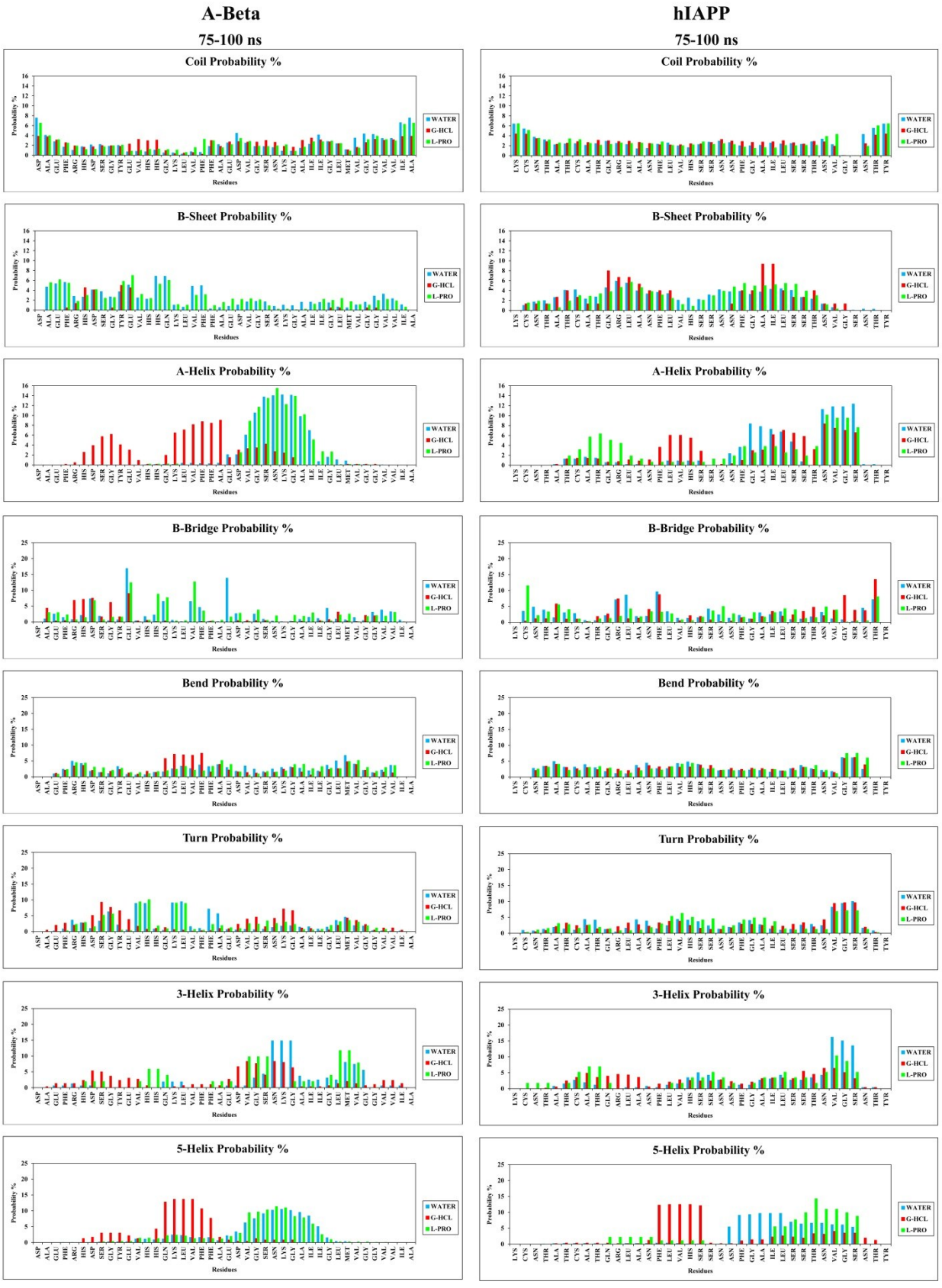

A-Beta
75-100 ns
hIAPP
75-100 ns
Coil Probability %
B-Sheet Probability %
A-Helix Probability %
B-Bridge Probability %
Bend Probability %
Turn Probability %
3-Helix Probability %
5-Helix Probability %
Probability %
Residues
WATER
G-HCL
L-PRO

Figure S7

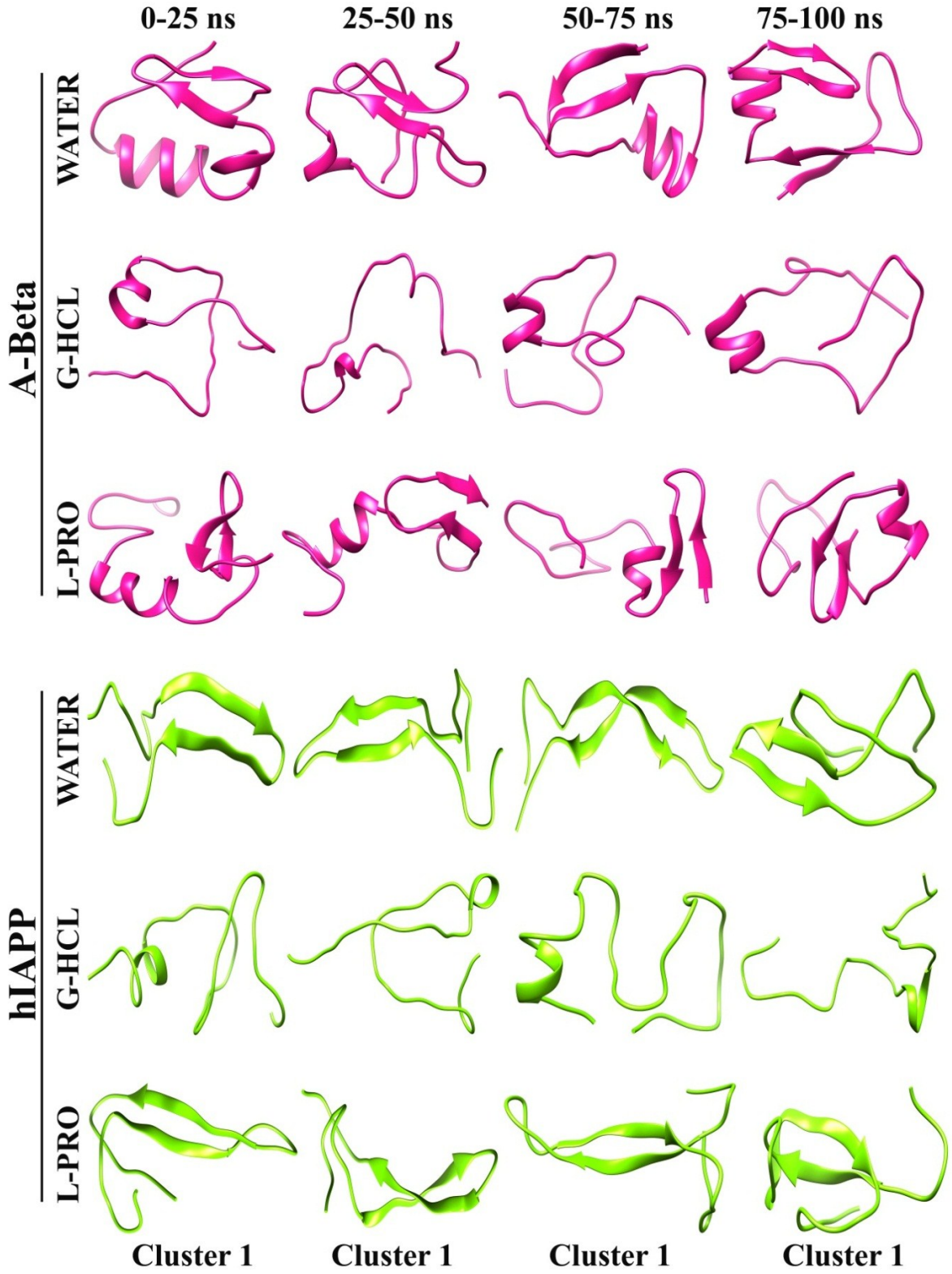

0-25 ns
25-50 ns
50-75 ns
75-100 ns
A-Beta
WATER
G-HCL
L-PRO
hIAPP
WATER
G-HCL
L-PRO
Cluster 1
Cluster 1
Cluster 1
Cluster 1

Figure S8

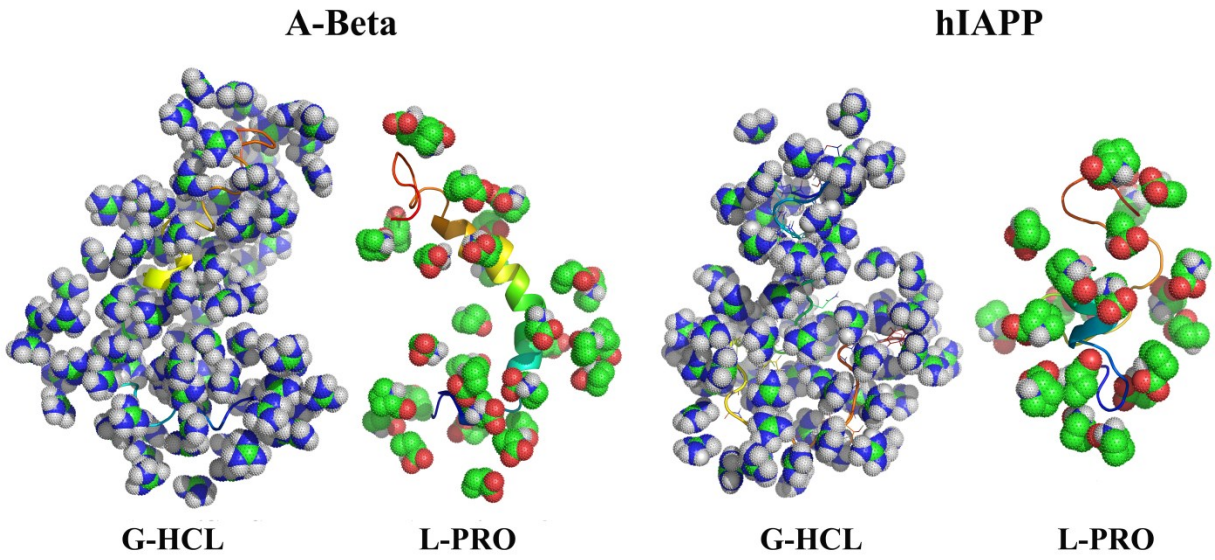


Figure S9


(A)
A-Beta/G-HCL
A-Beta/L-PRO
0-25 ns
25-50 ns
50-75 ns
75-100 ns
Number of Osmolytes
Residues
0.25 - 0.50 nm
0.50 - 0.75 nm
0.75 - 1.00 nm
(B)
hIAPP/G-HCL
hIAPP/L-PRO
0-25 ns
25-50 ns
50-75 ns
75-100 ns
Number of Osmolytes
Residues
0.25 - 0.50 nm
0.50 - 0.75 nm
0.75 - 1.00 nm

Figure S10*A*

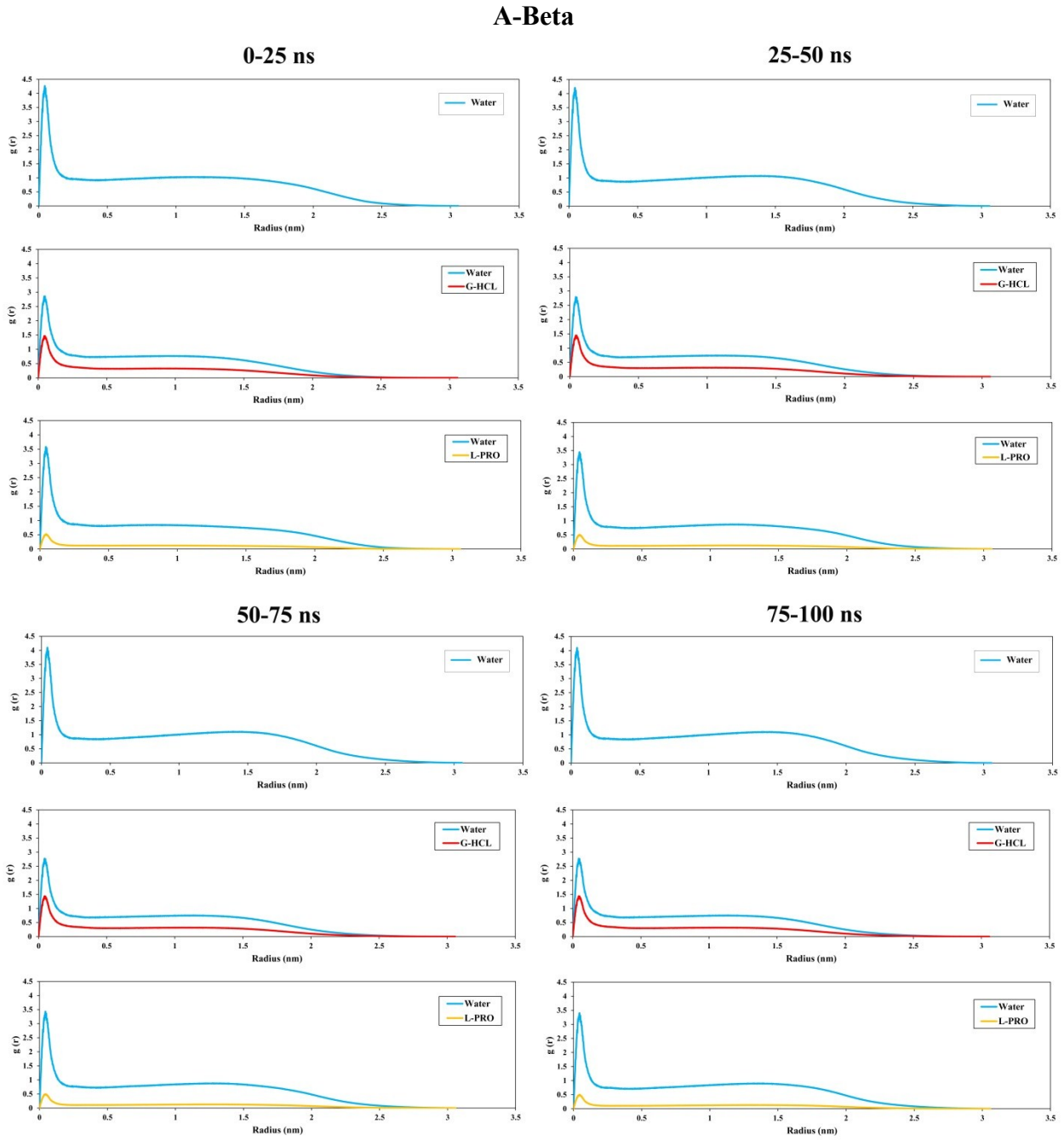
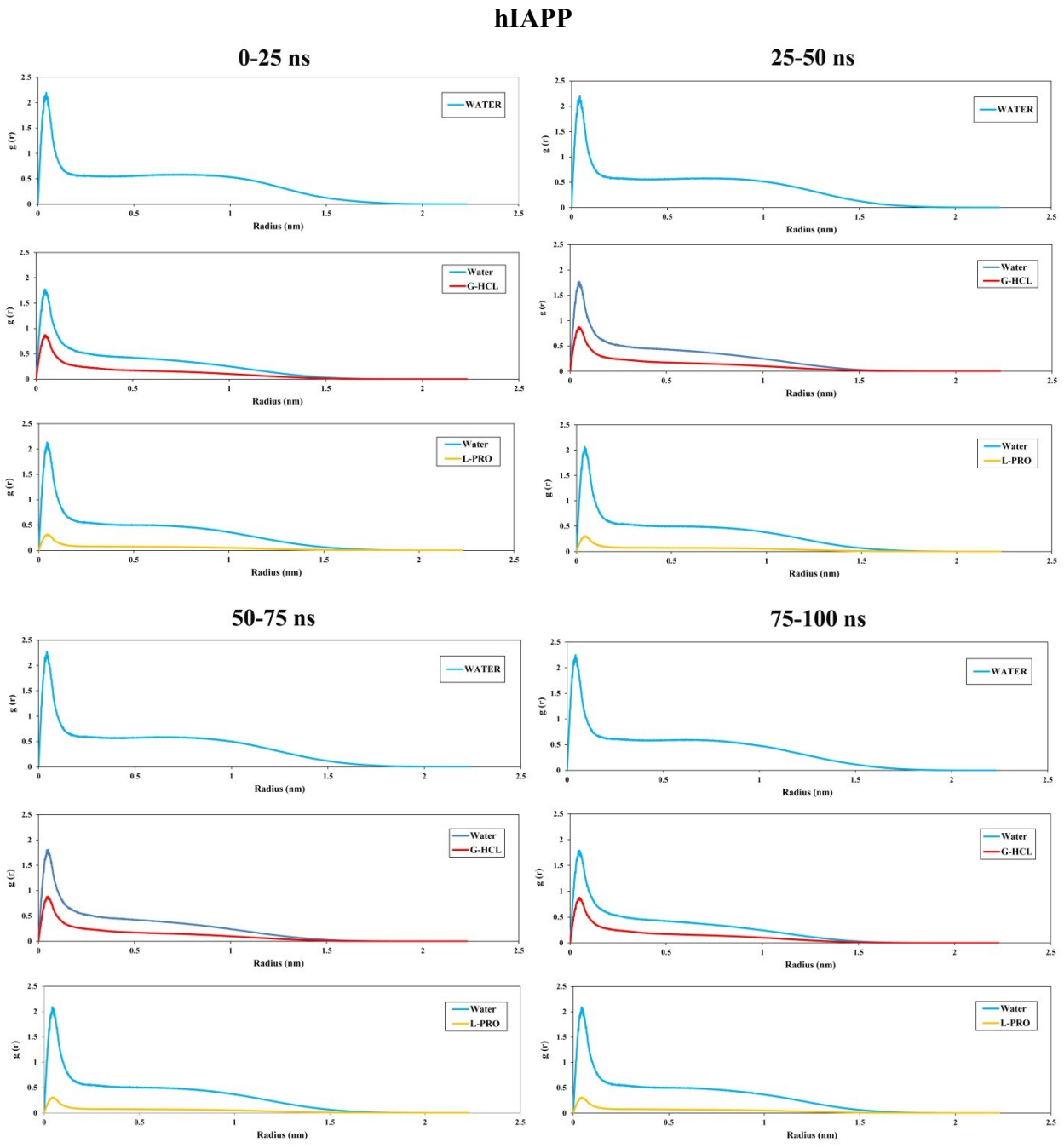

A-Beta
0-25 ns
25-50 ns
50-75 ns
75-100 ns
Water
G-HCL
L-PRO
g (r)
Radius (nm)

Figure S10*B*


hIAPP
0-25 ns
25-50 ns
50-75 ns
75-100 ns
WATER
Water
G-HCL
L-PRO
g (r)
Radius (nm)