Table S1. Structures found in our simulations have N-terminal helix conformations similar to solved crystal structures.

|  |  |
| --- | --- |
| **Ref. Protein (PDB ID)** | **RMSD** |
| ApoE2 (1LE2) [1] | 3.188 Å |
| ApoE3 (1NFN) [2] | 2.361 Å |
| ApoE3 (1OR3) [3] | 2.265 Å |
| ApoE3 (1OR2) [3] | 2.096 Å |
| ApoE3 (1LPE) [4] | 2.754 Å |
| ApoE3 (1BZ4) [3] | 2.714 Å |
| ApoE4 (1B68) [5] | 2.924 Å |
| ApoE4 (1GS9) [6] | 2.809 Å |
| ApoE4 (1LE4) [1] | 3.247 Å |

Root mean square deviation (RMSD) of the centroid the most populated clusters of ApoE isoforms’ conformations from local minima on the PMF-derived free energy landscapes at 275K. RMSD is computed over the Cα of the N-terminal domain helices. The C-terminal domain is not available in any of the ApoE crystal structures.