Supporting Information for

Using *in silico* click chemistry to design novel dopamine D3 receptor ligands as blood-brain barrier permeants

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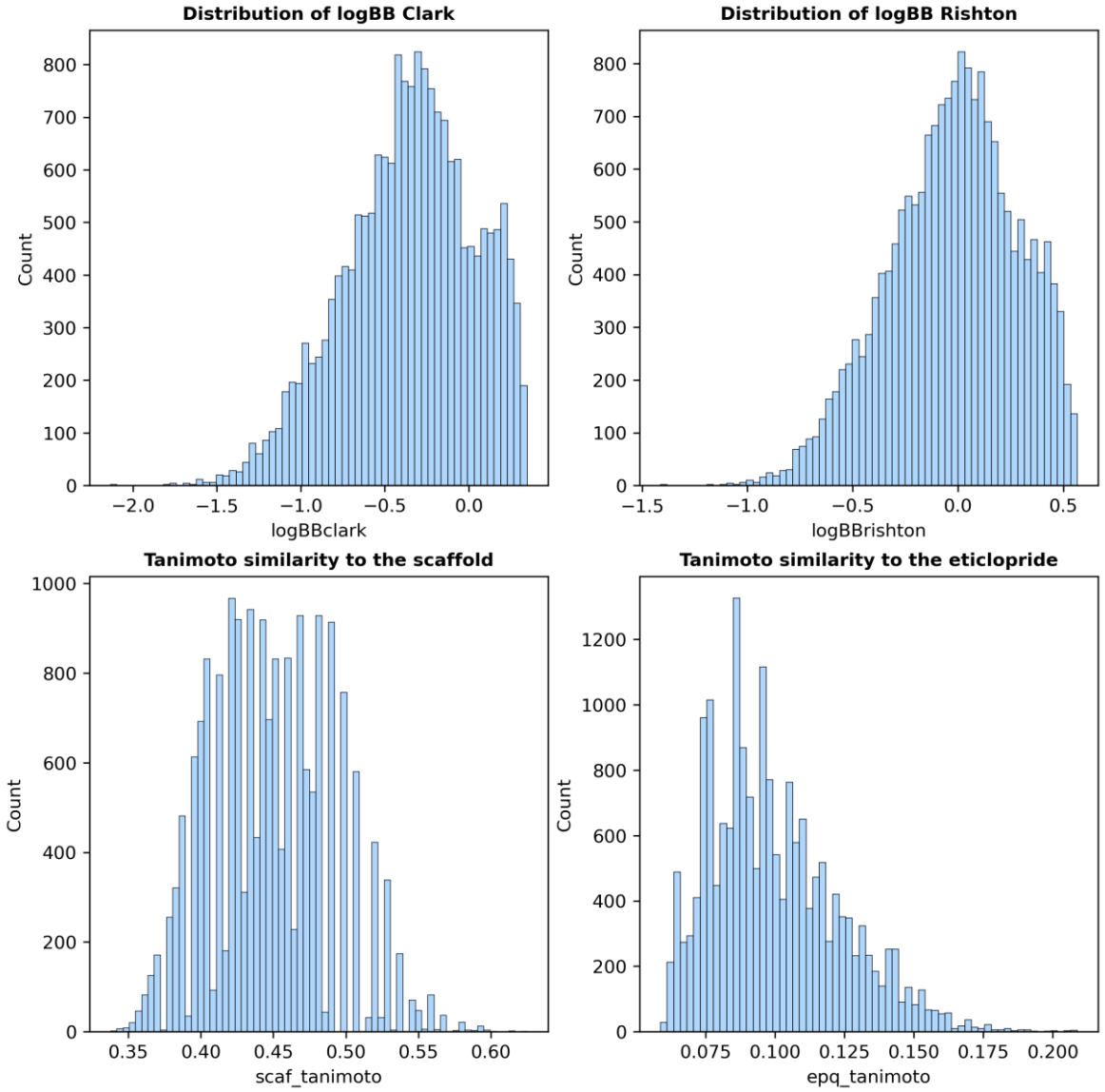

Figure S1. Distributions of logBB calculated with Clark and Rishton equations, and Tanimoto similarities to reference scaffold and eticlopride for the library of 18,838 molecules constructed by virtual click reaction.

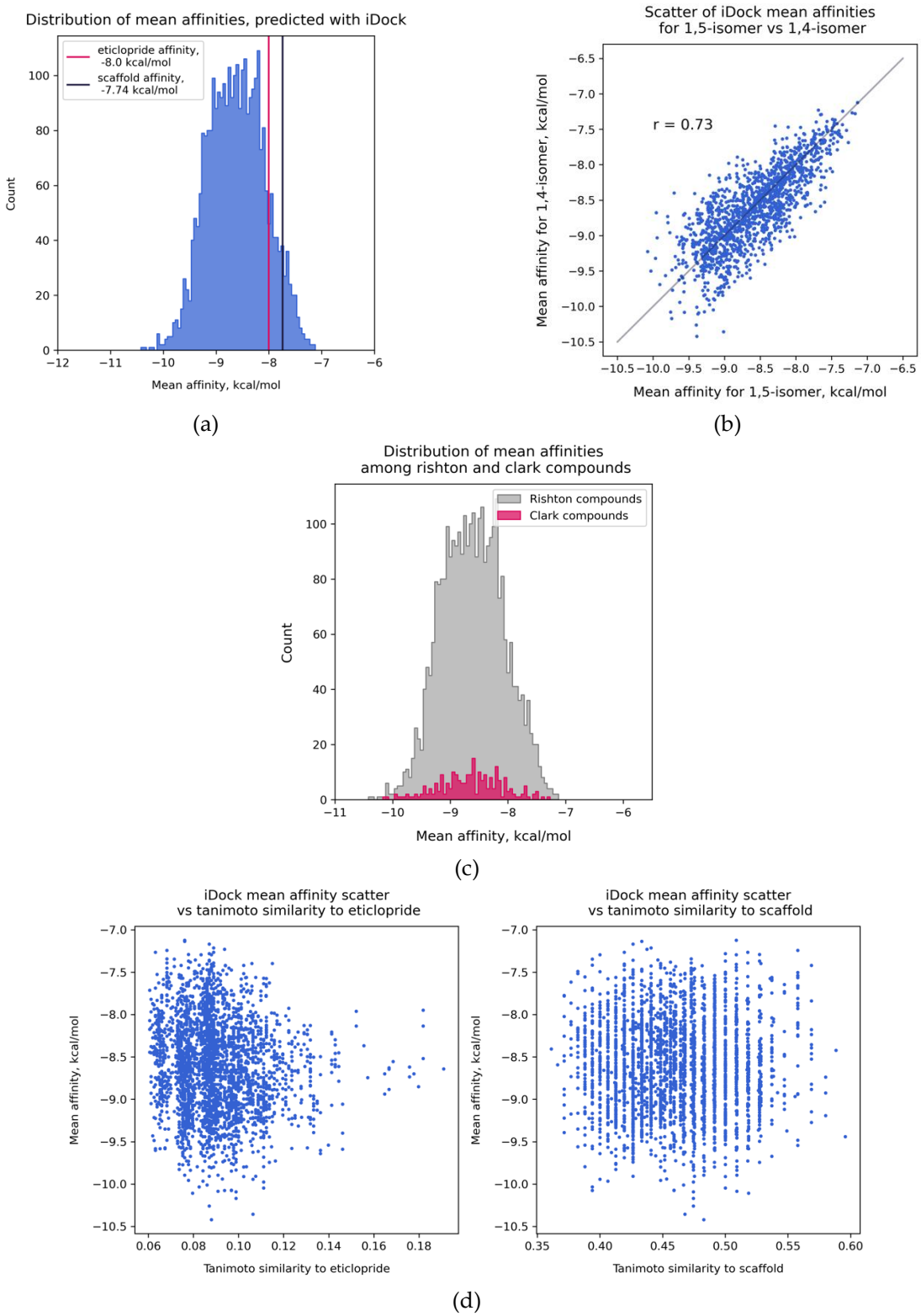

Figure S2. (**a**) Distribution of the mean affinities predicted by iDock with mean affinities for reference compounds, eticlopride (red line) and the scaffold (balck); (**b**) The scatter plot of iDock mean affinities in kcal/mol for 1,5-isomer molecules against values for 1,4-isomers of the same molecules (Pearson correlation coefficient r = 0.3); (**c**) Distribution of the mean affinities predicted with iDock with hue by groups of molecules passing Clark (red) and Rishton (gray) logBB filtering; (**d**) On the left, the scatter plot of iDock affinities in kcal/mol against molecules Tanimoto similarity to the eticlopride. On the right, the scatter plot of iDock affinities in kcal/mol against molecules Tanimoto similarity to the scaffold molecule

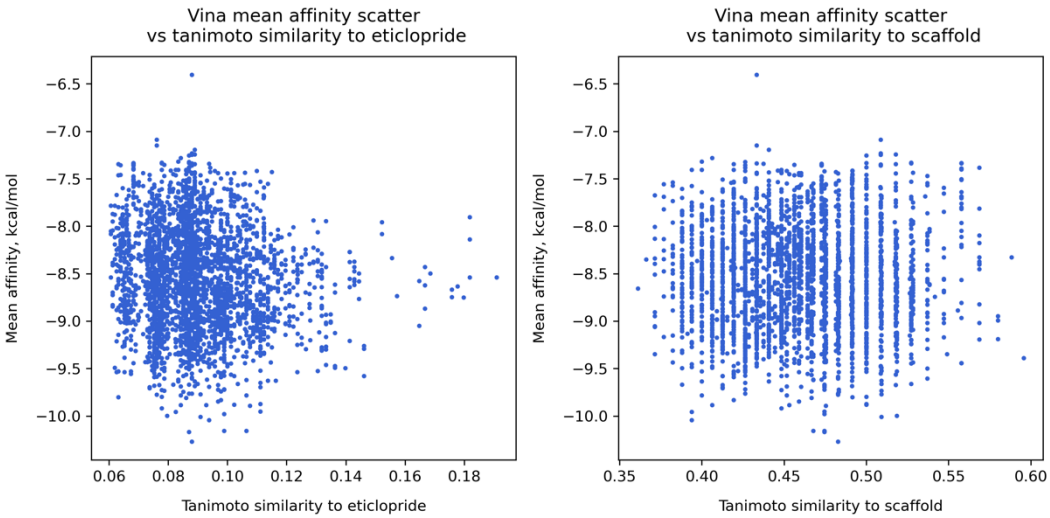

Figure S3. On the left, the scatter plot of Vina affinities in kcal/mol against molecules Tanimoto similarity to the eticlopride. On the right, the scatter plot of Vina affinities in kcal/mol against molecules Tanimoto similarity to the scaffold molecule

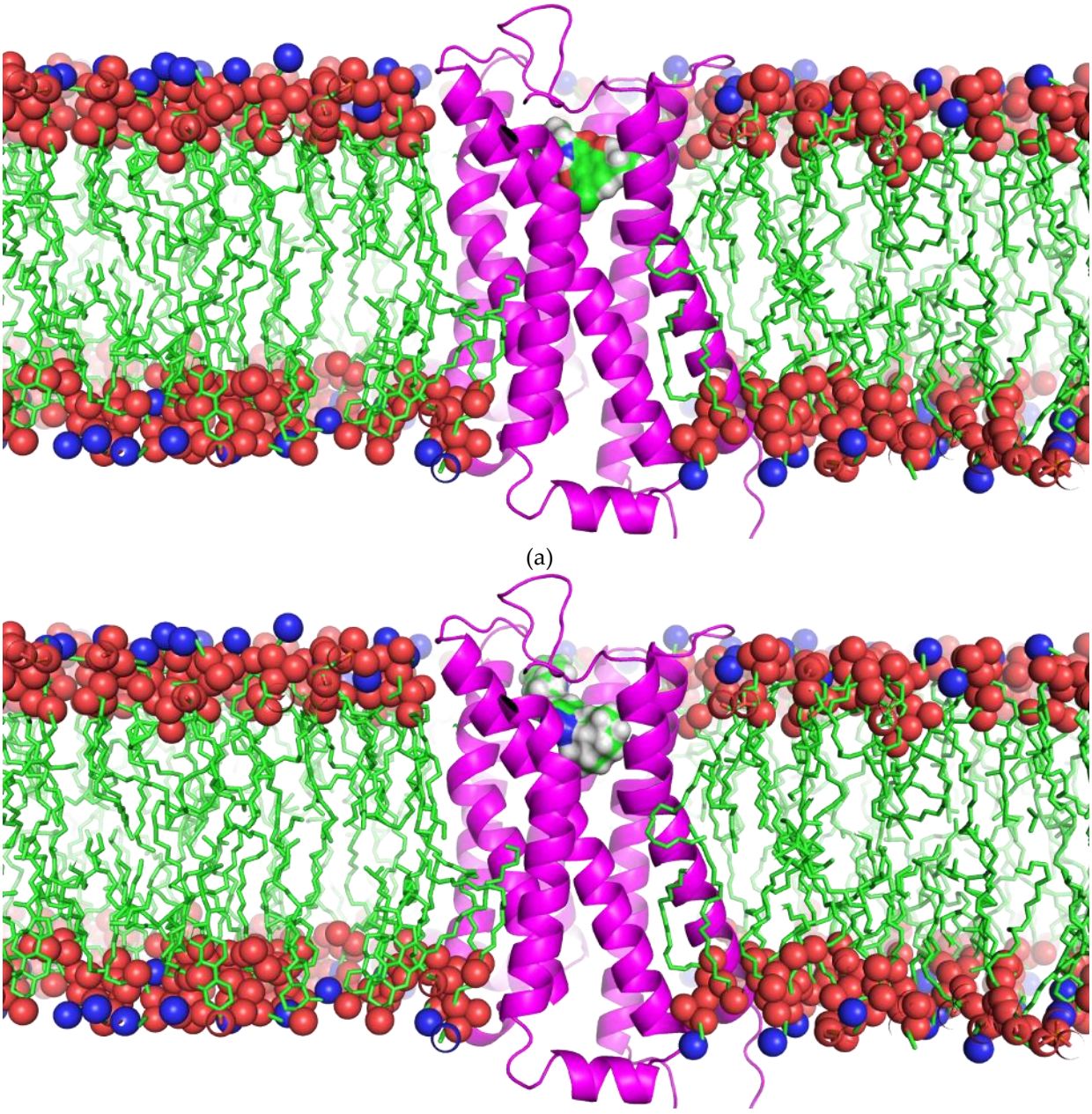

Figure S4. Full-atom D3 receptor models embedded into the lipid membrane with (**a**) bound eticlopride or (**b**) novel hit, id 7000. The molecules are colored according to their atomic composition. The membrane and protein are depicted as stick and cartoon models, respectively. The nitrogen and oxygen atoms are visualized as blue and red spheres. The ligands are represented using high-resolution molecular surface. The hydrogen atoms are omitted (except for ligand) to enhance clarity.