



**Supporting Information S5 Fig. Flexibility of individual residues of hA<sub>2A</sub>R.** MD-averaged PAD indexes [1] of the receptor in **I** (blue line), **II** (green) and **III** (red). Large PAD values indicate large flexibility for individual residues [1]. The panels in blue, green and red indicate residues belonging to the transmembrane helices H1-H7, to the loops and to the amphipathic helix H8, respectively.

#### Supporting References

1. Caliendo R, Rossetti G, Carloni P (2012) Local fluctuations and conformational transitions in proteins. *Journal of Chemical Theory and Computation* 8: 4775-4785.